“CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH PROGNOSIS IN ORGANOPHOSPHORUS POISONING”

Dissertation submitted in partial fulfillment of the

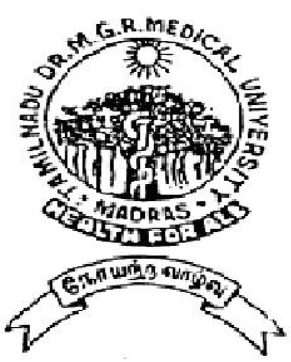
Requirement for the award of the Degree

of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

APRIL 2012



THE TAMILNADU

DR.M.G.R. MEDICAL UNIVERSITY

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CERTIFICATE

This is to certify that the dissertation entitled **"CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH PROGNOSIS IN ORGANOPHOSPHORUS POISONING"** is a bonafide work of **Dr.A.SHANMUGASUNDARAM,** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine Branch I examination to be held in April 2012.

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DECLARATION

I, **Dr. A.SHANMUGASUNDARAM,** solemnly declare that, this dissertation **"CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH PROGNOSIS IN ORGANOPHOSPHORUS POISONING"** is a bonafide record of work done by me at the Department of General Medicine, Government Rajaji Hospital, Madurai, under the guidance of **Dr.M.NATARAJAN M.D.,** Professor, Department of General Medicine, Madurai Medical college, Madurai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Degree of Doctor of Medicine (M.D.), General Medicine Branch-I, examination to be held in April 2012.

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ACKNOWLEDGEMENT

I would like to thank **Dr.EDWIN JOE, M.D.,** Dean, Madurai Medical College,for permitting me to utilise the hospital facilities for the dissertation.

I also extend my sincere thanks to **Prof.Dr.MOSES .K.DANIEL M.D,** Head of the Department and Professor of Medicine for his constant support during the study.

I would like to express my deep sense of gratitude and thanks to my Unit Chief, my guide and Professor of Medicine, **Dr.M.NATARAJAN M.D.,** for his valuable suggestions and excellent guidance during the study.

I express my sincere thanks to **Dr.R.A.JANARTHANAN, M.D., D.M.,** Professor & HOD,Dept.of Cardiology for permitting me to utilise the facilities of the Department for the purpose of this study and guiding me with enthusiasm through out the study period.

I thank the Assistant Professors of my Unit **Dr.G.SELVARANI M.D., D.H.Sc (Echo)** and **Dr.K.MURALIDHARAN, M.D.** and Assistant Professors of Department of Cardiology **Dr.S.NAINA MOHAMED M.D.,D.M., Dr.S.R.VEERAMANI M.D.,D.M., Dr.N.GANESAN M.D.,D.M.** and **Dr.G.S.SIVAKUMAR M.D,D.M** for their valid comments, guidance and suggestions.

I wish to acknowledge all those, including my Post graduate colleagues, my parents and my wife who have directly or indirectly helped me complete this work with great success.

Last but definitely not the least, I thank all the patients who participated in this study for their extreme patience and co-operation.

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1.INTRODUCTION

Organophosphorus compounds have assumed considerable importance in most parts of the world particularly developing countries but also in western countries.[1] Hospital based statistics suggest that nearly half of the admissions in emergency with acute poisoning are due to Organophosphorous compound poisoning.[2] The toxicity of those compounds and paucity of appropriate medical facilities lead on to a high fatality rate. These compounds first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control.[3] Organophosphorous compound poisonings are found to be a leading cause of death in agricultural countries globally.[4-5]

Their easy accessibility along with socio-cultural factors play a considerable role in the selection of Organophosphates as a main suicidal poison and is most often preferred by young economically productive age group with a case fatality ratio around 20 percent. WHO estimates about 3 million people are being exposed to pesticide poisoning every year with about 2,00,000 deaths per year in developing countries.[6] . India has the highest incidence of OP poisoning in the world. Nearly 90% of the poisoning are suicidal with a fatality rate of >10% ; 8-10% accidental

and <1% Homicidal. Occupational exposure accounts for 1/5th of accidental poisoning with fatalities of <1%.[7]

The organophosphorous compounds are the organic derivatives of phosphorous containing acids. The phosphonate, which are organic derivatives of phosphoric acid are, not used as insecticides but are used as chemical warfare agents. Organophosphorous compounds combine with esteratic sites of acetyl cholinesterase, that is phosphorylated & phosphorylated esteratic sites undergo hydrolysis. The phosphorylated enzyme is inactive and thus unable to hydrolyze acetylcholine. The biological effects of organophosphorous compound are as a result of accumulation of endogenous acetylcholine at sites of cholinergic transmission. This causes disruption of transmission of nerve impulses in both peripheral and central nervous system. Most organophosphorous compounds are readily absorbed through respiratory, oral and gastrointestinal mucous membrane, and through intact skin, as they are lipid soluble. This binding is irreversible, except with early pharmacological intervention.[8]

The diagnosis is based on the history of exposure and features of cholinergic overactivity.[9] The treatment includes atropine or glycopyrrolate, which acts as a physiological antidote and oximes which help in reactivating the enzyme.

Complications like respiratory failure, CNS depression and ventricular arrhythmias should be anticipated and treated.

Cardiac manifestations often accompany poisoning with these compounds including, hypotension, hypertension, sinus bradycardia, sinus tachycardia & cardiac arrest. Electrocardiographic changes reported in previous studies include Sinus tachycardia, Sinus bradycardia, QTc prolongation, ST-T changes, along with various forms of arrhythmias, which may be serious and fatal. These complications are potentially preventable, if recognized early and treated adequately**.** Organophosphate poisoning has been postulated both in animal and human studies to cause myocardiotoxic damage (myocardial necrosis). Electrocardiographic changes in organophosphate compound poisoning have been reported along with the associated structural myocardial damage. Organophosphate compound poisoning itself causes diarrhoea and vomiting which can lead to electrolyte derangements which by themselves may impart electrocardiographic changes.

Thus, this study is undertaken to study the electrocardiographic changes of organophosphate poisoning, which is so far much less studied and evaluate the importance of these changes in organophosphate compound poisoning considering the mortality and sufferings of those patients.

2.REVIEW OF LITERATURE

HISTORICAL REVIEW

Organophosphorous compounds and carbomates that were first discovered more than 100 years ago, are at present the predominant groups of insecticides employed globally for pest control. The compounds are toxic to humans and represent an important source of poisoning domestically, in some occupation or when ingested as a suicidal agent.[5]

During the past four decades, more than 35,000 different formulations have come into use as pesticides.[14] Of these, organophosphorous insecticides are possibly the most widely used in the world. The majority of the Patients (79% in a study) were less than 30 years of age.[15]

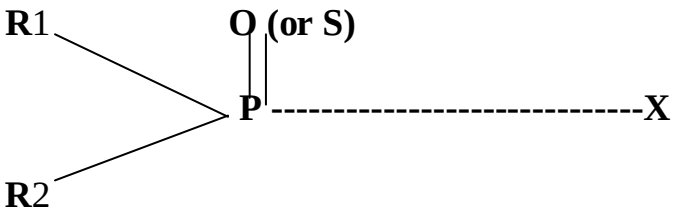
Modern investigations of organophosphorous compound date from 1932 when Lange and Krugger recorded the synthesis of dimethyl & diethyl phosphofluoridates. They noted that these compounds caused a persistent choking sensation and blurring of vision. This observation led Schrader of I.G. Farben industries to develop organophosphorous compound, first as agricultural insecticides and later as potential chemical warfare agents. Consequently, during World War II, several toxic compounds were developed and used as nitrogen gases

in Germany.[16] In 1991, these very compounds formed the cornerstone of Iraq's much-dreaded chemical warfare arsenal during the Gulf war. Organophosphorous compound first came to India in 1951, to be used as insecticides and in 1962 first Organophosphorous poisoning was reported in India.[17]

CHEMISTRY

Organophosphorous compounds are usually esters /amides of thiol derivatives of phosphoric / phosphonic acids.

The General formula being:



Where,

R1 and R2 are usually simple alkyl or aryl groups.

X is known as the "leaving group" may be one of a wide variety of substituted or branched aliphatic, aromatic or heterocyclic groups linked to phosphorous via a bond of some liability usually –O-or -S-.

The double bonded atom may be O or S and the related compound, termed a phosphate or phosphorothioate.[7]

CLASSIFICATION

Holmstedt proposed a classification system for organophosphorous that is of pharmacological and toxicological interest.

The compounds are divided into 5 groups with a few relevant examples.[16]

Group A: (X: Halogen, Cyanide, and Thiocyanate)

E.g.: Disopropylophosphate fluoridate (DFP)

Isopropyl methyl phosphofluoridate (SARIN)

Pinacolyl Methyl phosphofluoridate (SOMAN)

Group B: (X: Alkyl, alkoxy, aryloxy)

E.g.: Forstenon, DDVP, Pyrazoxon

Group C: (X: Thiol or Thiophosphorous Compound)

E.g.: Parathion, Malathion, Azethion, Diazinon, Systox, and Demeton

Group D: (Pyrophosphates and related compounds)

E.g.; TEPP, DPDA, OMPA

Group E: (Quaternary Ammonium Compound)

E.g.: Phospholin

An older more commonly used classification divides these compounds into:

1) Alkyl phosphates (Eg. TEPP, HETP, OMPA, Malathion, Systox, DFP etc).

2) Aryl Phosphates (Eg. Demeton, Parathion, EPN, Chlorothion, Diazinon, etc).

PHARMACODYNAMICS & METABOLISM:

These compounds are generally dispersed as aerosols /dusts, consisting of organophosphorous compound absorbed to an inert finely particulate material. Therefore practically all routes including gastrointestinal tract, skin and mucous membranes following contact with the liquid form, rapidly and effectively absorb these compounds. The lungs also absorb them, after inhalation of the vapors or finely dispersed dusts/ aerosols.

Following absorption they quickly distribute in all tissues, maximum concentration usually being reached in the liver and the kidneys. Lipophilic compounds may reach high concentration in neural and other lipid rich tissues.

Plasma half-life ranges from few minutes to few hours, depending on the compounds and route of administration.

Metabolism occurs primarily by oxidation. Parathion is converted to biologically active compound – "Paroxon" by microsomal activation in the liver.

Malathion is metabolized to inactive compound more rapidly in higher animals, and consequently is less dangerous to man.

Highly lipid soluble agents such as Chlorfenthion may produce symptoms and signs of cholinergic over activity for an extended period of days to weeks, caused by subcutaneous lipid storage followed by subsequent chronic systemic

release after redistribution. These compounds also cause repeated release after apparently successful management.

Detoxification of the organophosphorous insecticides occurs, either by bio-chemical modification of their structure or by linkage to the binding site without toxicological significance.

Elimination of organophosphorous compounds and their metabolites occur mainly through urine and faeces, with 80-90% of most of compounds being eliminated within 48 hours. A very small portion of organophosphorous compounds and their active forms are excreted unchanged in the urine.

Some compounds are known to persist in the body for longer periods.

MECHANISM OF ACTION

Anticholinesterases bind to and inhibit a number of enzymes, yet it is their action on the esterase which is of clinical importance.[7]

a. Inhibition of Acetylcholinesterases (Ach E)

Acetylcholinesterases (AchE) are responsible for the hydrolytic cleavage of Acetylcholine (Ach) to choline and acetic acid. Acetylcholine is a neurotransmitter for all postganglionic autonomic fibers, postganglionic parasympathetic fibers, postganglionic sympathetic fibers, neuromuscular junction and some interneuron synapses in the CNS. A potential reaction causes release of acetylcholine in the

presynaptic cleft, most of which is degraded by acetylcholinesterases. Acetylcholine, which is not degraded, binds to the postsynaptic receptors resulting in the generation of an excitatory postsynaptic potential and propagation of the impulse.

Anti-acetylcholinesterase has two sites namely, anionic and esteratic site. Acetylcholine binds to the anionic site on acetylcholinesterases and undergoes hydrolysis in a few seconds. The reversible Anti-acetylcholinesterases combine with acetylcholinesterases at the anionic site and this blocks attachment of the substrate.[19]

Irreversible Anti-acetylcholinesterases on the other hand binds to the esteratic site of the Acetylcholine and inhibit irreversibly thereby phosphorylating it. This leads to accumulation of acetylcholine at the synapses with initial overstimulation followed by inhibition of synaptic conduction.

Following inhibition, reactivation of the enzyme (acetylcholinesterase) occurs at the rate of 1% per day by slow de novo synthesis of fresh enzyme and also by spontaneous dephosphorylation.[20]

The rate of inactivation (phosphorylation) and reactivation (dephosphorylation) depends of the species and the tissue in addition to the chemical group attached accounting for the differences in toxicity.[21]

Response to reactivating agents decline with time, a process referred to as '**aging**' of the inhibited enzyme. It is a result of loss of an alkyl or alkoxyl group leaving a much more stable monoalkyl or monoalkoxyl phosphoryl acetylcholinesterase.[18] The aged phosphorylated enzyme cannot be reactivated by oximes.[22] In chemical warfare agents like soman, aging occurs rapidly.[20]

b. Inhibition of Neuropathy target esterase:

Neuropathy target esterase (NTE) inhibition followed by its transformation to an aged form is responsible for the organophosphate- induced delayed neuropathy (OPIDN).[23]

PATHOPHYSIOLOGY

Acetylcholine is a neurotransmitter released by the terminal nerve endings of all postganglionic parasympathetic ganglia.

There are three types of acetylcholinesterase enzyme present in the body; in red blood cells or true cholinesterase, serum pseudocholinesterase and brain cholinesterase.[24] True cholinesterases are found primarily in nervous tissues and erythrocytes, while pseudo cholinesterases are present in plasma, liver and non-neuronal tissues. Pseudo cholinesterase levels helps to diagnose a case of suspected poisoning.[7]

The pathophysiological effects of organophosphates result from inhibition of ChE (both RBC and pseudo cholinesterase). These are the markers of exposure, acute toxic effects and reflect actual activity at cholinergic nerve terminal.[111]

In the acute phase of OP poisoning serum ChE activity is usually depressed within few hours to days and is also restored to normal levels quickly. About 3% of the population has a genetic variation manifested by a serum ChE deficiency. Pregnancy, acute (or) chronic inflammatory conditions,malnutrition and liver disease are conditions that also affect serum ChE levels, but the depression caused by these conditions are not as great as those caused by the organophosphate insecticides. This level can vary from person to person. A 50% reduction in ChE[50,75] levels from the baseline may result in acute cholinergic symptoms of organophosphate exposure. These values differ among laboratories, and the range is very wide, with a 30% spread.[112]

OP pesticides inhibit AchE at muscarinic and nicotinic synapses by depositing a phosphoryl group at the enzymes' active site to form a temporary covalent bond which results in the accumulation of Ach and uncontrolled activation of cholinergic synapses. Over time, one of two processes will occur. The covalent bond may spontaneously cleave leaving the enzyme functional again. This process may take upto 1000 hours. Meanwhile the enzyme is prone to "**Ageing**" in

its active site in which one of the "R" group may cleave non-enzymatically, leaving a hydroxyl group in its place. Aged AChE with its negatively charged phosphate can no longer be attacked by a nucleophile, i.e. OH or an oximate group. And regeneration is no longer possible. Recovery of a functional pathway must wait until new ChE enzyme is manufactured, a process that may take weeks. The time it takes for ageing to occur varies according to the specific pesticide, but takes no longer than 48 hours. Clinically the toxic effects of OP agents may persist more than a week.[113] Oximes slows down "ageing" of the phosphorylated cholinesterase and binds to the OP agent, making it non reactive. This results in ChE regeneration and a rise in serum levels of ChE.[111]

CLINICAL FEATURES

The clinical manifestations of organophosphorous poisoning are a result of cholinergic over activity and can be divided into the effects of over stimulation of the muscarinic, nicotinic and CNS receptors.[5]

The clinical diagnosis is based on:

a. history of exposure

b. The presence of several of the symptoms and signs such as garlic odour, secretions, miosis, fasciculations, respiratory failure etc as to be discussed below.

The time interval between the exposure and onset of symptoms and signs varies with the route and degree of exposure. The interval maybe within 5 minutes after massive ingestion and is almost always less than 12 hours. The severity of manifestation varies with the degree of poisoning.

In recent works, it has been reported that children, particularly less than nine years of age manifest “nicotinic” signs rather than “muscarinic” signs of poisoning. The most common features of paediatric poisoning are CNS depression and hypotonia.[113]

Namba et al[9] have made a classification of organophosphorous poisoning insecticide which is modified from Grob et al[25] and is as follows: -

Latent poisoning: -

No clinical manifestations are seen. Diagnosis based on estimation of serum cholinesterase activity, which is inhibited by 10 to 50%

Mild poisoning: -

The patient complains of fatigue, headache, dizziness, nausea, vomiting, excessive sweating, salivation, chest tightness, numbness of extremities, abdominal cramps or diarrhea. Serum cholinesterase levels are 20-50% of normal values.

Table 1: Clinical features according to receptor stimulation

Muscarinic Receptors	Nicotinic Receptors	Central Receptors
CVS	**Muscles**	
Bradycardia	Fasciculations	Altered Consciousness
Hypotension	Weakness	Respiratory Depression
	Paralysis	Cheyne– Stokes Respiration
GIT	Cramps	Dysarthia
Salivation	**CVS**	Tremors
Nausea	Tachycardia	
Vomiting	Hypertension	
Abdominal Pain		
Diarrhea		
Tenesmus		
Feacal Incontinence		
RS		
Bronchorrhea		
Wheezing		
Cough		
Eye		
Miosis		
Lacrimation		
Skin- moist		

Moderate poisoning: -

The patient complains of generalized weakness, difficulty in talking, muscular fasciculations and miosis. Serum cholinesterase levels are 10-20% of normal values.

Severe poisoning: -

Marked miosis, unconsciousness, loss of pupillary reflex to light, muscular fasciculation, flaccid paralysis, and secretions from the mouth and nose, rales in the lungs, respiratory difficulty and cyanosis are seen in patients with severe poisoning. Serum cholinesterase levels are lower than 10% of normal values.

However, this proposed grading has proved unworkable in clinical practice because of many varied clinical criteria in different grades, as well as the difficulty in remembering and applying them in acute clinical situation.[5, 12]

The second classification was proposed by **Bardin et al**[12] and is as follows: -

Grade 0 Nil	Positive history
	No signs of organophosphorous poisoning.
Grade 1 Mild	Mild secretions,
	Few fasciculations,
	Normal level of sensorium.
Grade 2 Moderate	Copious secretions,
	Generalized fasciculations,
	Rhonchi, crepitations,
	Hypotension (systolic BP <90mmHg)

		Disturbed level of consciousness, not stuperous
Grade 3	Severe	Stupor, PaO2 < 50mmHg, Chest roentgenogram abnormal.

This study by Bardin et al showed that patients with grade 3 manifestations on admission were associated with increased requirement for mechanical ventilator. The presence of other complications and increased days of ICU stay have been observed in the above patients.

Grading of Fasciculation was done by giving 1 point depending on the presence of fasciculations each to the anterior chest, posterior chest, anterior abdomen, posterior abdomen, right thigh, left thigh, right leg, left leg, right arm and left arm. The total Fasciculation score is thus estimated.

Following organophosphorous poisoning three well-defined clinical phases[7] are seen:

1. Initial acute cholinergic crisis.
2. The intermediate syndrome
3. Delayed Polyneuropathy (OPIDN-Organophosphorous Induced Delayed Neuropathy)

In addition chronic organophosphate induced neuropsychiatric disorder (COPIND) can occur.

1. Acute cholinergic phase:

This is the initial phase of acute poisoning resulting in muscarinic and nicotinic effects. The accumulation of acetylcholine at the muscarinic site produces an increase in secretions. Bronchorrhea, salivation, sweating, bradycardia, vomiting and an increase in gastro-intestinal motility (abdominal tightness and cramps). In the eye, organophosphorous agents cause the diagnostic miosis which results in blurring of vision. The effects of increased acetylcholine at nicotinic sites. Eg: The neuromuscular junction, cause muscle fasciculation. Inhibition of acetylcholinesterase in the brain leads to headache, insomnia, giddiness, confusion and drowsiness. After severe exposure, slurred speech, convulsions, respiratory depression and coma occur.

The mechanism of action for muscle paralysis is depolarization and desensitization blocks induced by acetylcholine at the neuromuscular junctions. Death is likely during this initial cholinergic phase due to effects on the heart like bradycardia, arrhythmias; respiratory failure and depression of vital centers in the brain. Cases with even vocal cord paralysis have been reported.[49] Bradycardia may be severe and may progress to heart block. The cholinergic phase usually lasts 24

to 48 hours and constitutes a medical emergency that required treatment in an ICU.[20]

2. Intermediate syndrome

Senanayake and Karallieda first coined the term “Intermediate syndrome” in 1987.[28] After recovery from the cholinergic crisis, but before the expected onset of delayed polyneuropathy, some patients develop a muscle paralysis, which is described as Intermediate syndrome. This phenomenon has been reported in between 20-68% of the patients.[29]

The development of IMS might be due to a conformational change in the acetylcholine receptor altering depolarizing neuromuscular block to a non-depolarising block characterized by a fade on tetanic stimulation.

The cardinal feature of this syndrome is muscle weakness affecting predominantly the proximal limb muscle and neck flexors. Motor cranial nerve palsies (III to VII and X) also occur. Respiratory muscle weakness leading to respiratory failure could lead to a fatal outcome. Deep tendon reflexes are usually depressed. The intermediate syndrome occurs after recovery from the cholinergic crisis within 24 hours to 96 hours but before the expected onset of the delayed neuropathy, which occurs 2 to 3 weeks after the poisoning.[4]

Complete recovery occurs within 4 to 18 days, if adequate ventilator support is provided. The agents commonly responsible are fenthion, monocrotophos, dimethoate, diazinon and methyl parathion.[30]

3. Delayed Polyneuropathy

The neuropathy develops following latent periods of 2-4 weeks after the cholinergic crisis. The cardinal symptoms are distal muscle weakness, calf pain preceding the weakness and in some cases paraesthesia in the distal parts of the limbs. Weakness initially appears in the leg muscles causing foot drop, followed by small muscles of the hands. Later it may extend proximally and even involve the truncal muscles. Deep tendon jerks are absent. The prognosis of patients with mild neuropathy is good but those with severe neuropathy are usually left with persistent deficits that are claw hand, foot drop, persistent atrophy, spasticity and ataxias.

Delayed Polyneuropathy is common following exposure to organophosphorous compounds, which have weak anticholinesterase activity Eg. Triorthocresylphosphate. The occurrence of Delayed Polyneuropathy appears to follow phosphorylation and subsequent aging of an enzyme in axons called as neuropathy target esterase (NTE). The function of this enzyme is not clear yet. It is however present in the brain, spinal cord and the peripheral nervous system. NTE is a membrane bound protein with high esterase catalytic activity. This

phosphorylation enzyme also undergoes ageing.[31] The agents commonly responsible are mepafox and chloropyrifos.[32, 33, 34, 35]

Chronic Organophosphate Induced Neuropsychiatric Disorder (COPIND)

Behavioral effects have been documented following acute or chronic organophosphorous poisoning. These include,

a. Impairment of vigilance, information processing, psychomotor speed and memory.

b. Poor performance and perception of speech.

c. Increased tendency to depression, anxiety and irritability.

d. A tendency to faster frequencies and higher voltages in EEG.

Extra pyramidal manifestations (dystonia, rest tremors, cogwheel rigidity and chorea-athetosis)[35] may occur four to forty days after organophosphorous poisoning. Recent studies suggest that Parkinson's disease is a more common in patients who report to have had previous exposure to pesticides.[36]

INVESTIGATIONS

1. Arterial blood for oxygen and carbon dioxide partial pressures.

2. Venous blood for estimation of red cell acetylcholinesterase and concentration of the OP compound.

3 . Venous blood for estimation of biochemistry (electrolytes, glucose, amylase, lipase, creatinine) and haematology.

4. Chest X-ray.

5.Ultrasound scan of the abdomen (pancreatic status).

DIAGNOSIS

Diagnosis depends on the following factors:

a. History or evidence of exposure to anticholineserase agents.

b. Signs and symptoms of poisoning.

c. Improvement of these clinical features with atropine and PAM.

d. Inhibition of cholinesterase activity.

In most patients, a history of exposure to organophosphorous insecticide can be obtained. A container is usually found. History may be denied in attempts of suicide or unavailable in-patients who are found unconscious. Organophosphates impart a garlic-like odour to the breath, vomitus or faeces.[7] The signs of organophosphorous poisoning that are most helpful in diagnosis are miosis and muscle fasciculations. Others include excessive perspiration, salivation, Lacrimation and bronchial secretion.[7, 9]

The response to atropine therapy may also be useful aid to diagnosis, with patients who have organophosphorous poisoning showing a tolerance to atropine.

There is also failure to produce signs of atropinisation with 1 to 2mg of atropine administered intravenously.[5]

Inhibition of cholinesterase activity(50% reduction considered confirmatory) of the blood is also helpful. Estimation of erythrocyte cholinesterase (acetyl cholinesterase) is theoretically preferred as it reflects the degree of inhibition of synaptic cholinesterase. However, estimation of plasma cholinesterase (pseudo cholinesterase) can be done.[7, 5]

Estimation of blood sugar and urine acetone can help ruling out Diabetic ketoacidosis since it is an important differential diagnosis of OP poisoning, yet OP consumption itself may cause hyperglycemia. Serum amylase level is said to raise and has prognostic significance. X ray chest can clearly show pulmonary congestion and edema indicating the severity of poisoning.

Methods used for assay for AchE activity vary in sophistication. They include the classical electrometric method, the calorimetric method and a titrometric assay.

TREATMENT

All patients should be managed as emergencies in hospital.

A. Acute Cholinergic Crisis: [7]

Treatment is based on the following principles:

a. Minimizing further absorption of the insecticide.

b. Pharmacologically countering the effects of the poison.

c. Maintaining vital functions.

Successful management requires rapid and simultaneous implementation of the above principles.

First aid measures should include removal of patient from the contaminated environment, removal of contaminated clothes and washing of the skin and eyes.

Respiratory failure is the usual cause of death in the acute phase; resuscitation and artificial respiration may be required immediately. Mouth-to-mouth respiration should not be attempted.

Cardiac arrhythmias include various degrees of heart block and should be managed accordingly.

Gastric lavage is most effective within 30 minutes of ingestion but is advised also at the time of admission after taking necessary precautions to protect the airway, adequate oxygenation and supportive invasive ventilation if needed. If the patient is semiconscious/unconscious, Ryle's tube aspiration can be done. Activated charcoal, 1g/kg dose every 2-4 hours may be administered to reduce further absorption from the stomach except in cases of intestinal obstruction featured by absent bowel sounds, tense rigid abdomen.

Atropine:

Treatment with anticholinergic medication is still the mainstay of treatment and should be started as soon as the airway has been secure. Full early atropinisation is an essential and simple part of an early management and a delay can result in death from central respiratory depression, bronchospasm, bronchorrhoea, severe bradycardia or hypotension.

Atropine acts as a physiological antidote, effectively antagonizing the muscarinic-receptor-mediated action. It has virtually no effect against the peripheral neuromuscular dysfunction and subsequent paralysis induced by organophosphorous agent.

A recommended dose is 2-4 mg intravenous, repeated at interval of 5-10 minutes initially and continued until signs of **atropinisation** (dry axillae, clear lungs, no miosis, flushing of skin, systolic BP > 80 mm Hg and a heart rate of > 80 beats/ minute) appear. Atropine therapy should be maintained until there is complete recovery. The maintenance dose is said to be about 10% of the dose needed for atropinisation as continuous infusion and needs to be adjusted according to the toxic features on observation.

Table 2: Atropine Recommendations

SOURCE	RECOMMENDED REGIMEN FOR ATROPINISATION	MARKERS OF ATROPINISATION
Harrison's Internal medicine 18th Edition, 2011	0.5mg repeated every 5-15 min	Dry secretions
Australian medicines hand book 14th Edition, 2003	2mg iv repeated until atropinisation is achieved then infusion titrated against clinical effects	Abolish all secretions
British national formulatory edition -46, 2003	2mg repeated every 5-10 min. IM or IV according to severity	Dry flushed skin, dilated pupils, tachycardia
WHO model formulatory edition -1, 2002	2 mg repeated every 20-30 min	Flushed early skin and tachycardia

Infusion of atropine are used in some centers in dose of 0.02-0.08 mg/kg/hr.[51] Infusion of atropine has produced significant reduction in mortality in some centers when compared to conventionally intermittent therapy.[52] A heart rate exceeding 140 beats/minute should be avoided. ST-segment abnormalities in the ECG may be induced by large doses of atropine.[74] These may be corrected with propronalol, eliminating any need to reduce the rate of administration of atropine. Atropine crosses the blood brain barrier and may cause severe toxic effects such as convulsions, psychosis and coma,[53] which if necessary should be corrected using Physostigmine

Glycopyrrolate:

This is a quaternary ammonium compound that can be used as an alternative to atropine. The advantages of Glycopyrrolate over atropine are: -

a. Better control of secretions .[54]

b. Less tachycardia.[55]

c. Fewer CNS side effects.[56]

Oximes:

The observation that oximes reactivates phosphorylated AchE more rapidly than spontaneous hydrolysis led to the development of Pralidoxime (Pyridine-2-aldoxime methyl chloride, PAM) and later Obidoxime, Trimedoxime, Asoxime, HI6, HIo7 etc.

The reactivating action of pralidoxime[78] is most marked at the skeletal neuromuscular junction. It acts by reactivation of the inhibited phosphorylated enzyme to free the active form. Its dose is 500 mg/hour for severe poisoning and 1gm 8-12 hourly for mild to moderate poisoning in adults and 25-50 mg/kg in children, given intravenous in 250ml normal saline over 30 minutes. The WHO recommended Pralidoxime regimen is 30 mg/kg bolus followed by 8 mg/kg infusion. It has no effect on the muscarinic effect. It has short half-life of 1.2 hours when given intravenous[57] and does not cross the blood brain barrier.[16]

PAM should be administered as early as possible,[26] at least within 4-36 hours of poisoning for regeneration of AchE. It is dependent primarily on the life span of the erythrocytes when aging of the enzyme has occurred.[20]

PAM is available as chloride, iodide, mesylate and methyl sulfate salts. The chloride salt is more stable than iodide in dry state and is preferred for intramuscular use.

The major pharmacological action of oximes is to reactivate AchE by removal of phosphate group bound to the esteritic site.[5] This action occurs shortly after poisoning and inhibition of the enzymes, after which the enzyme ages and becomes more firmly bound to esteratic site.[58] Oximes should be given as soon as possible before aging takes place. They are most effective if given within 6 hours of poisoning, but beneficial response is seen upto 24 hours of poisoning.

The therapeutic effects of oximes seemed to depend on the plasma concentrations of the organophosphorous agent with the benefit being, minimal at high concentrations of organophosphorous in the blood. Pralidoxime does not cross the blood-brain barrier whereas obidoxime does.

Paradoxically high doses of pralidoxime may cause neuromuscular block and other effects including inhibition of AchE.[16] High frequencies of cardiac

arrhythmias were observed in patients who received high cumulative doses of atropine and Obidoxime.

Diazepam:

Some reports have indicated that benzodiazepines are useful as antidotes in poisoning by anticholinesterases.[59] This appears to counteract some aspects of CNS derived symptoms and also increase therapeutic effects of atropine and PAM.

Diazepam is used to treat convulsions after organophosphorous poisoning and in the support of ventilatory care

Fluoride:

Fluoride and atropine combination produces a greater antidotal effect than atropine alone.[20] It was noted that increased cholinesterase levels were observed in workers in a plastic factory handling fluoride compounds.

Magnesium:

Kiss and Fazekas[44] reported that ventricular premature contractions were successfully eliminated with intravenous magnesium sulfate. The magnesium was thought to counteract direct toxic inhibitory effect of organophosphates on sodium-potassium ATPase.

Phenothiazines:

The use of phenothiazines in the management of organophosphorous poisoning is controversial. Diazepam has proved to be satisfactory and popular alternative.[7]

Respiratory stimulants:

Respiratory stimulants should not be used in the treatment of organophosphorous poisoning in humans, particularly, in view of the bronchospasm, neuromuscular block and convulsions that are associated with intoxication.[60]

Other measures:

Dialysis of blood against activated charcoal (hemoperfusion) is effective in demeton-S-methyl sulphoxide, dimethoate and parathion poisoning.[61] Prompt improvements have been reported following repeated injections of purified lyophilised human cholinesterase.[19] Resealed cells containing a recombinant phosphotriesterase provided protection against the lethal effect of paraoxon. Phosphotriesterase hydrolyses paraoxon to the less toxic 4-nitrophenol and diethylphosphate. This enzyme was encapsulated into carrier erythrocytes by hypotonic dialysis with subsequent resealing and annealing. The encapsulated enzyme was found to persist longer and possess much greater efficacy. When these

carrier cells were administered in combination with pralidoxime chloride and atropine, a marked synergism was observed. The use of fresh plasma and exchange transfusions are of little value. Corticosteroids, camphor, potassium chloride, clonidine and vitamin C have been used with varying degree of success. However, all these regimens need further evaluation.[7]

Management of Intermediate Syndrome:[7]

Prompt and effective management of respiratory insufficiency is the cornerstone of treatment of Intermediate syndrome.

Patients should be observed for early signs of respiratory failure and facilities for ventilatory care should be made available. Frequent blood-gas analyses are useful in monitoring and weaning from ventilatory support. Diazepam in 10 mg intravenous doses may be useful in anxious or restless patients on ventilator.

Management of Delayed Neuropathy:[7]

No specific drug therapy has proved useful. The muscle weakness benefits from regular exercise and physiotherapy.

Complications

Complications resulting from organophosphorous poisoning occur in about 43% of cases with acute intoxication.[12, 62]

Death can often occur early (within 24hours) in untreated cases and upto 10 days in hospital with optimal management.[63]

Early deaths are due to CNS depression, seizures, and ventricular arrhythmias (Eg. Torsade de pointes) or respiratory failure due to excessive bronchial secretions, pulmonary edema, aspiration pneumonia, respiratory muscle paralysis or respiratory center depression.[10, 27]

Late mortality is caused by respiratory failure[11, 12] associated with infection (pneumonia, septicemia) or ventilator related complications.

There are various studies in which **respiratory failure** was the commonest complication encountered following acute organophosphorous poisoning.[64, 65]

The pathogenesis is multifactorial and related to aspiration of gastric contents, excessive secretions in the airways, pulmonary infections, pneumonia, septicemia and development of ARDS.[11]

Respiratory consequences of muscarinic overstimulation including rhinorrhoea, bronchorrhea, bronchoconstriction and laryngeal spasm may

contribute to respiratory failure. These are often combined with nicotinic effects such as respiratory muscle weakness and paralysis (including paralysis of tongue and nasopharynx).

Central depression of respiratory centre occurs following cholinergic overstimulation of synapses in the brain stem and is a prominent cause of hypoxia, respiratory failure and death in the early period of acute organophosphorous poisoning.[10]

Peripheral neuromuscular block producing respiratory muscle weakness and paralysis as well as the recently described intermediate neuropathy[28] contributes to the development of respiratory insufficiency at a later stage.

Sudden cardiovascular collapse is often the first indication of unsuspected or incipient respiratory failure, a presentation that is associated with a high mortality.[11]

The development of **pneumonia** is the most important cause of delayed respiratory failure after organophosphorous poisoning and this occurs in upto 43% of the patients.[11, 13, 62] Upto 80% of patients with pneumonia had respiratory failure; majority of these could be diagnosed within 96 hours of poisoning.[11]

Inadequate or delayed atropinisation appears to be one of the principle reasons for the development of pneumonia[12] and emphasis the importance of skilled medical assessment and treatment at an early stage after poisoning.

Prevention:[7]

Preventive measures should be considered at all the levels of the chain of insecticide movement through the environment-formulation manufacture, mixing application and disposal.

Psychiatric counselling for prevention of second episode should always be given. General counseling and drug therapy for depression should be added. Strict guidelines should be adopted during transport and storage to prevent contamination of food, clothing, drugs, toys, cosmetics and furnishing.

Other effects of organophosphorous intoxication

Altered immunity to infection

In 1974, Bellin and Chow[37] suggested that organophosphorous agents might have an effect on the human immune system. Casali et al[38] demonstrated that parathion suppressed both the primary IgM and IgG response to sheep erythrocytes in mice.

Newcombe[39] showed an increased incidence of lymphoproliferative disorders associated with impaired natural killer cell and cytotoxic T-cell function.

Murray et al[40] reported influenza like symptoms in 23 patients after occupational exposure to organophosphorous compounds.

Changes in metabolism and endocrine activity

In animal experiments, changes in the diurnal pattern of plasma ACTH have been reported following organophosphorous poisoning.[41] Nicotinic receptors also function in brain pathway that increases the release of several pituitary hormones including vasopressors, ACTH and prolactin. In man, nonketotic hyperglycemia may occur.[42, 43]

Effects on Reproduction

There is a report of termination of pregnancy following organophosphorous poisoning during the first trimester.[47] In experimental animals, organophosphorous poisoning during pregnancy cause pre- and postnatal death and congenital abnormalities such as vertebral deformities, limb defect, polydactyl and cleft palate.

GI effects

Profuse diarrhea for 2 to 5 days after ingestion of organophosphorous insecticides has been reported.

Temperature Regulation

After exposure to most organophosphorous compounds, a marked hypothermia response lasting upto 24 hours has been demonstrated.[48]

Effects on Cardiovascular system

The mechanism by which organophosphates induce cardiotoxicity is still uncertain. **Ludomirsky et** al[79] described three phases of cardiac toxicity after OP poisoning:

Phase 1 Brief period of increased sympathetic tone

Phase 2 Prolonged period of parasympathetic activity

Phase 3 QTc prolongation followed by torsades de pointes ventricular tachycardia and then ventricular fibrillation.

Both these autonomic overactivities have been shown to cause myocardial damage.[80, 81] Possible other mechanisms include hypoxemia, acidosis, electrolyte derangements and a direct toxic effect of the compounds on the myocardium.

Some investigators[79, 82] described a polymorphic ventricular tachycardia of the torsades de pointes attributed to prolonged QTc interval. High dose atropine has also been implicated to cause ventricular arrhythmias.[83, 84] But Ludomirsky[79] and Lyzhnikov[80] et al both found no correlation between atropine therapy and VT in OP poisoning.

Hypertension and sinus tachycardia are nicotinic while hypotension and sinus bradycardia are cholinergic manifestations.[85] Though bradycardia dominate the early cholinergic phase, sinus tachycardia was a more frequent finding in many studies.[86, 87, 88] Some consider hypertension and tachycardia to be indicators of severe poisoning.[9]

Cardiac complications of OP poisoning are not fully appreciated by many physicians. Mostly they occur during few early hours of poisoning for which the patient should be transferred immediately to ICU or CCU where proper resuscitative facilities are available. Intensive supportive treatment, meticulous respiratory care, and administration of atropine in adequate doses very early are the keys to manage cardiac toxicity of OP compounds.

The management of ventricular arrhythmias in OP poisoning is difficult and therapy has included, electrical cardioversion, lidocaine, bretylium and overdrive

pacing(for tachycardias),[12] and intravenous isoproterenol, magnesium and pacing (for brady-cardias).[17,20,21] In one report of severely intoxicated patients, complete replacement of blood (to provide acetylcholinesterase) resulted in the disappearance of arrhythmias and normalisation of the QT_c.

QT prolongation

QT interval is a measure of the time between the start of the **Q wave** and the end of the **T wave** in the heart's electrical cycle. In general, the QT interval represents electrical depolarization and repolarization of the left and right ventricles. A prolonged QT interval is a biomarker for ventricular tachyarrhythmias like torsades de pointes and a risk factor for sudden death.

The QT interval is dependent on the heart rate in an obvious way (the faster the heart rate the shorter the QT interval) and may be adjusted to improve the detection of patients at increased risk of ventricular arrhythmia. A quick but rough assessment to find QT prolongation is that, if QT is more than half of the R-R interval, it is supposed to be prolonged. The standard clinical correction is to use ***Bazett's formula***,[89] named after physiologist Henry Cuthbert Bazett, calculating the heart rate-corrected QT interval *QTc*.

Bazett's formula is as follows:

$$QTcB = QT / \sqrt{RR}$$

where **QTc** is the QT interval corrected for heart rate, and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex, *measured in seconds*, often derived from the heart rate (HR) as 60/HR (here QT is measured in milliseconds). However, this nonlinear formula, obtained from data in only 39 young men, is not accurate, and over-corrects at high heart rates and under-corrects at low heart rates.[90]

Fridericia[91] has published an alternative correction using the cube-root of RR.

$$QTcF = QT / 3\sqrt{RR}$$

There are several other methods as well. For example a regression-based approach that had been developed by

Sagie et al[92], as follows:

$$QTcL = QT + 0.154(1000 - RR)$$

Normal QT duration is **0.35 to 0.43**[93] adjusted to a heart rate of 60/min.

Prolongation of the QT interval can be categorized into primary and secondary forms.

Primary(Congenital) QT prolongation includes underlying gene mutations that result in ion channel malfunction and congenital long QT syndromes.[94] Based on

the malfunction, the long QT syndromes (LQT) can be due to overabundance of sodium inflow or inadequate potassium outflow, resulting in excessive positive intracellular ions and delayed ventricular repolarization, like

Jervell-Lange-Neilson syndrome (JLN1-2) - deafness, syncope and sudden death

Romana Ward syndrome (LQT 1-6) - no deafness

Anderson syndrome (LQT 7) - skeletol abnormalities like short stature, scoliosis etc.

Timothy syndrome (LQT 8) - congenital heart disease, musculoskeletol disease, immune dysfunction

Secondary (acquired) QT prolongation[95, 96] can be attributed to

Altered nutrition (anorexia nervosa, starvation diets, alcoholism)

Bradycardia (< 50 beats/min)

Cerebrovascular disease (intracranial and subarachnoid hemorrhage, stroke, intracranial trauma)

Diabetes mellitus

Elderly age

Electrolyte disturbances (hypokalemia, hypomagnesemia, hypocalcemia)

Deep sleep

Heart failure (cardiomyopathy, dilated or hypertrophic)

Hypertension

Hypoglycemia

Hypothermia

Hypothyroidism

Myocardial ischemia or infarction[97, 98, 99]

Obesity

Poisoning (arsenic, organophosphates, nerve gas)

Pituitary insufficiency

Drugs – A huge drug list including Amiodarone, Chloroquine, Cisapride, Clarithromycin, Domperidone, Erythromycin, Terfinidine, Pimozide, Quinidine, Sotalol etc.

ST elevation

An ST elevation is considered significant if the vertical distance between the ECG trace and the isoelectric line at a point 0.04 seconds after the J-point is at least 1 mm in a limb lead or 2 mm in a precordial lead. This measure has a false positive rate of 15-20% (which is slightly higher in women than men) and a false negative rate of 20-30%.[100]

Causes for ST elevation goes by the mneumonic "ELEVATION"

E lectrolytes

L BBB

E arly Repolarization

V entricular hypertrophy

A neurysm

T reatment (e.g. pericardiocentesis)

I njury (AMI, OP poisoning, contusion)

O sborne waves (hypothermia)

N on-occlusive vasospasm (Prinzmetal angina)

Low Voltage Complexes

Diagnostic Criteria (Either of the below criteria may be met)[100]

Voltage of entire QRS complex in all limb leads <5mm.

Voltage of entire QRS complex in all precordial leads < 10mm.

Differential Diagnosis

An increase in the distance between the heart and the ECG leads, infiltration of the heart muscle itself and metabolic abnormalities are all associated with low voltage.

1. Increased Distance

Pericardial effusion

Obesity

COPD with hyperinflation

Pleural effusion

Constrictive pericarditis

2. Infiltrative Heart Disease

Amyloidosis

Scleroderma

Hemachromatosis

3. Metabolic Abnormality

Myxoedema

Inverted T Waves[100]

Normal finding in children

Persistent juvenile T wave pattern

Myocardial ischaemia and infarction

Bundle branch block

Ventricular hypertrophy (‘strain’ patterns)

Pulmonary embolism

Hypertrophic cardiomyopathy

Raised intracranial pressure

T wave inversion in lead III is a normal variant. New T-wave inversion (compared with prior ECGs) is always abnormal.

Pathological T wave inversion is usually symmetrical and deep (>3mm).

STUDIES ON ELECTROCARDIOGRAPHIC CHANGES IN OP POISONING

- Dalvi CP, Abraham PP, Iyer SS et al stated that Abnormal ST-T wave changes and progressive fall in voltage or low voltage were the commonest ECG changes encountered. Other ECG abnormalities, like prolongation of QT interval, Ectopic Beats, conduction defects and peaked P waves were seen less frequently. The dose of atropine required was highest and the rate of normalization of ECG and clinical recovery slowest, in the group with severe poisoning. The mortality was higher in moderate and severe groups, death was sudden and clinically unexpected in patient who were appearing to be recovering normally clinically. Abnormal ECG changes were present in 40% of mild cases, 87% of moderate cases, 100% of severe organophosphate poisoning cases .Patient with ECG changes should be monitored carefully till these changes revert back to normal because even after transient apparent clinical recovery, these patients are prone for sudden death[101].
- A M Saadeh, N A Farsakh, M K Al-Ali et al studied the frequency, extent and pathogenesis of cardiac complications accompanying organophosphate and carbamate poisoning. They concluded that cardiac complications often accompany poisoning with these compounds particularly during first few

hours. 46 cases records (24 females and 22 males) were reviewed. ECG manifestations were, prolonged QTc interval (67%), Elevated ST segment (24%), inverted T waves (17%) Prolonged PR interval (9%), Atrial fibrillation (9%), Ventricular tachycardia (9%), Extrasystoles (6%), Venticular fibrillation (4%). Other cardiac manifestations were noncardiogenic pulmonary oedema (43%), sinus tachycardia (35%), Sinus Bradycardia (28%), Hypertension (22%) and hypotension (17%). Hypoxemia, Acidosis and electrolyte derangements are major predisposing factors[86].

- S.B Agarwal, V.K Bhatnagar, Amol Agarwal, Usha Agarwal ,K.Venkaiah, S.K Nigam , S.K Kashyap et al studied complete clinical profile of organophosphate compound poisoning. In their study, sinus tachycardia, ST Segment depression and T wave Inversion followed by sinus bradycardia were the most common ECG abnormalities[102].
- P. Karki, J.A Ansari, S.Bhandary, S Koirala studied extent, frequency and pathogenesis of cardiac and electrocardiographic manifestation of acute organophosphate poisoning. They also studied clinical profile of organophosphate poisoning in terms of age, sex, intention, symptoms and signs, time interval between compound consumption and hospitalization, total dose of atropine given, duration of treatment with atropine, cardiac and

electrocardiographic manifestations. Cardiac manifestations and electrocardiographic changes were recorded before administration of any medications ECG manifestations in their study were prolonged QTc interval (37.8%), ST/T changes i.e. , Elevated ST segment (16.2%), inverted T waves (13.5%), Prolonged PR Interval (5.4%) Atrial fibrillation (5.4%), Ventricular tachycardia (10.8%), Extrasystole (5.4%). Other cardiac manifestations were sinus tachycardia (40.5%), Sinus bradycardia (18.9%), non cardiogenic pulmonary edema (21.6%), hypertension (13.5%), hypotension (10.8%). In this study cardiac complications developed in 62.2% of patients, most common being Sinus tachycardia (40.5%) and Prolonged QTc interval (37.8%)[103].

- Ismail Hamdi kara, Cahfer Guloglu, Aziz Karabulut, Murat Orak et al studied sociodemographic, clinical and laboratory features of cases of organophosphorus intoxication and found mean age of cases 24+/-11years, M/F ratio 1/3.8, mostly from low socioeconomical class and of suicidal intention, most common ECG changes were sinus tachycardia in 58.3%, ST changes in 54.2 % and T changes in 12.5%. Hypokalemia followed by hyponatremia were the most common Electrolyte Derangements seen in their study[104].

- Kumiko Taira,Yoshiko Aoyama and Miwako Kawamata studied relationship between ECG manifestations and subjective symptoms accompanying organophosphate pesticide exposure caused by aerial spray was investigated[105].
- Yurumez Y, Yavuz Y, Saglam H, Durukan P, Ozkan S, Akdur O, Yucel M evaluated 85 patients who presented to emergency department with Organophosphate poisoning and found QTc prolongation(55.5%) followed by sinus tachycardia (31.8%) were the most common Electrocardiographic changes[106].
- Another Indian Study by Manojith Mookherjee[2] from West Bengal (1999), conducted a retrospective analysis of 379 patients who were admitted over 8 years period with diagnosis of organophosphate compound poisoning. Cardiac complications developed in 197 (52%). These were: cardiac arrhythmia in 52%, prolonged QTc 46%, ST-T changes in 49% conduction defects in 5%, premature ventricular contractions in 67%, ventricular tachycardia in 2.1%, ventricular fibrillation in 0.52%, sinus tachycardia in 40%, bradycardia in 82%, hypotension in 15% and cardiac failure in 14% of patients.
- SC Chatterjee observed QTc prolongation(63.5%) followed by sinus tachycardia (37.5%) were the most common Electrocardiographic changes[107]

- In 1999 Mathur et al[3], from Jawaharlal Nehru Hospital, Ajmer reported ECG changes in 120 patients with organophosphate poisoning. Sinus tachycardia was the most common abnormality (99.33%) followed by ST-T changes (91.66%), QTc prolongation (35%) and conduction blocks (8.88%).

- Another study from Taiwan by Chuang et al[5] (1996), in 223 cases of organophosphate compound poisoning over 12 years reported the electrocardiographic changes which included, Q-Tc prolongation in 43.5% patients. These patients had higher mortality (19.6%) and higher incidence of respiratory failure. Q-Tc prolongation also correlated with severity of poisoning.

- Kiss and Fazekas[44] reported QT prolongation along with ST-segment, T-wave anomalies and other forms of arrhythmias. Recurrent ventricular tachycardia with the torsade de pointis phenomenon was seen. Complete atrioventricular block may occur.[45] QTc prolongation indicates a poor prognosis and a higher incidence of respiratory failure.[46]

3.AIM OF THE STUDY

- To study the Electrocardiographic changes associated with acute organophosphorous poisoning.
- To correlate these Electrocardiographic changes with the in-hospital course and prognosis of those patients.

4.METHODOLOGY

Subjects: Patients presenting with Organophosphorus poisoning were the study subjects.

Study Design: A prospective cross-sectional study.

Ethical committee approval: The Ethical committee approval was obtained to carry out the study in the hospital a copy of which is enclosed herewith.

Study place: Government Rajaji hospital, Madurai

Study Duration: April 2011 – September 2011

Study criteria

Inclusion Criteria:

All adult males and females with a history of exposure to organophosphorus compound within previous 24 hours with characteristic clinical manifestations of organophosphorus compound poisoning during the study period were included.

Exclusion Criteria:

1) Patients who received treatment with atropine before admission
2) Patients with doubtful diagnosis
3) Mixed poisoning with other substances
4) Known case of cardiac illness

5) Known case of long QT syndromes
6) Patients known to be taking drugs recently which are likely to prolong QT interval

Study protocol: A previously designed proforma was used to collect the demographic and clinical details of the patients.

Collaborating department:

Department of Cardiology, Government Rajaji Hospital, Madurai

Exposure Assessment

Demography

Age

Sex

Type of exposure

Agents used

Time interval from consumption to the time of admission

Mode of consumption

Poison particulars

Severity grading

Symptoms after consumption

Immediate steps taken after OP exposure

Clinical findings

Pupil size, mental status, secretions, fasciculations, convulsions, respiratory adequacy

Data collection

An ECG was recorded in each case as soon as possible (usually within 15 minutes) after admission. Treatment was not withheld in any case for the purpose of study.

Serial ECGs were obtained at 12 hour intervals (or earlier if any arrhythmia was detected clinically) during the period of stay in the hospital.

ECG analysis included the rate, rhythm, ST-T abnormalities, conduction defects and measurement of PR and QT intervals. The QT interval was corrected (QTc) according to the formula of Bazett

$$QTc = QT / \sqrt{RR}$$

where **QTc** is the QT interval corrected for heart rate, and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex, *measured in seconds*. The period of occurrence of such ECG changes were noted and the time of their normalization or death of patient whichever earlier were noted. The final outcome were registered as death or survival.

Those patients requiring ventilation due to respiratory failure or IMS and having prolonged hospital stay, and also patients dying during stay were excluded in the calculation of significance of ECG events with regard to inpatient stay.

About 112 patients fulfilling eligibility criteria were studied. Nearly 14 patients were excluded since they missed periodic ECG followup or brought dead before recording a single ECG.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.[76,77]

5.OBSERVATION AND RESULTS

Figure 1-Age distribution with OP poisoning

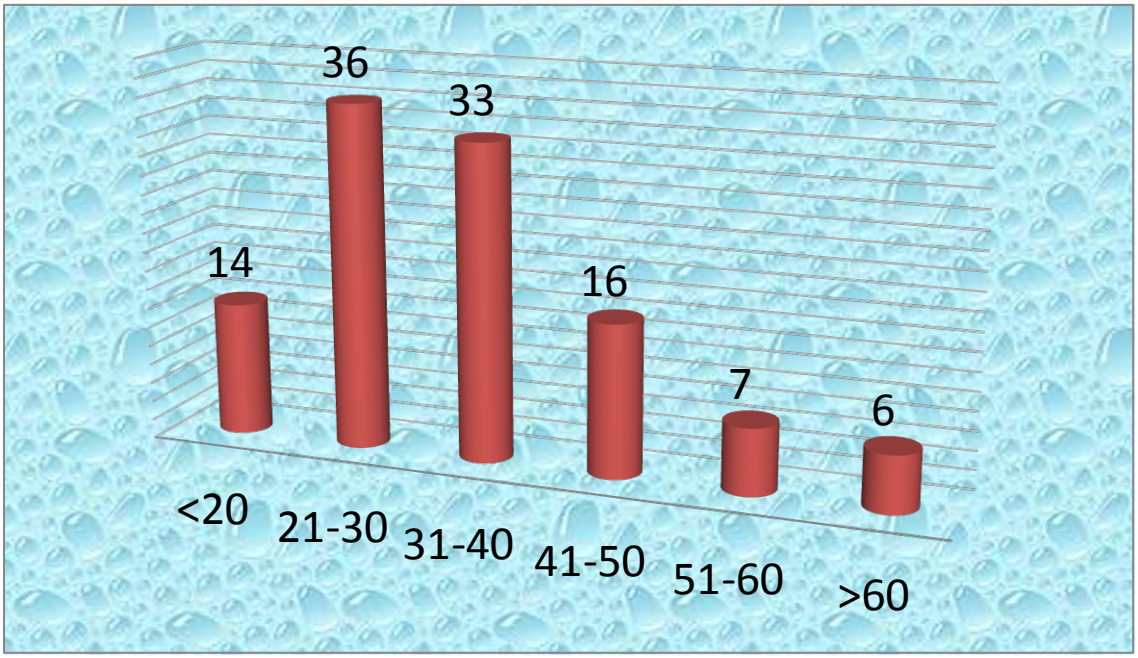


Figure 2-Sex distribution with OP poisoning

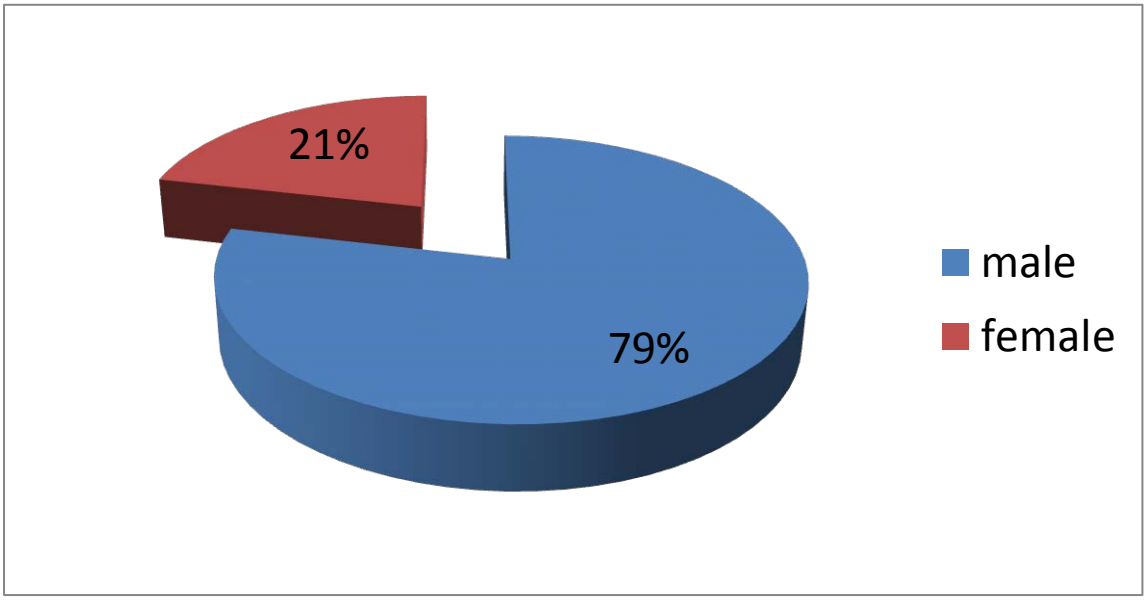


Figure 3-Mode of consumption

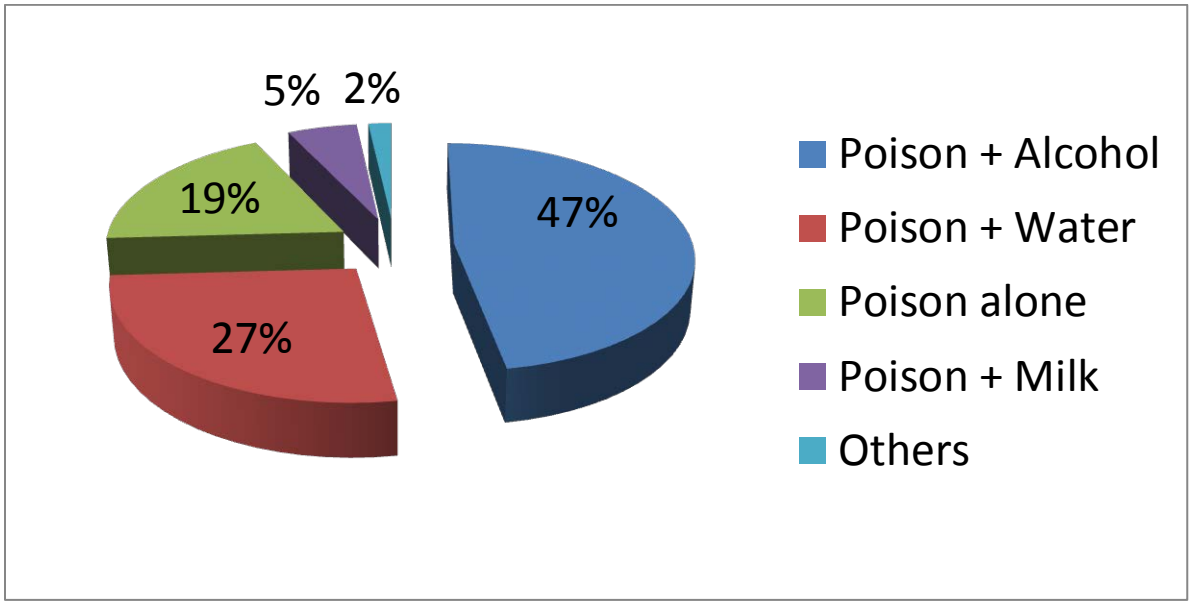


Table 3-Mode of consumption

Poison + Alcohol	Poison + Water	Poison alone	Poison + Milk	Others
23	13	8	3	2

Thus most patients used alcohol (23%) than water (13%) and others as vehicle

Figure 4-OP Agents consumed

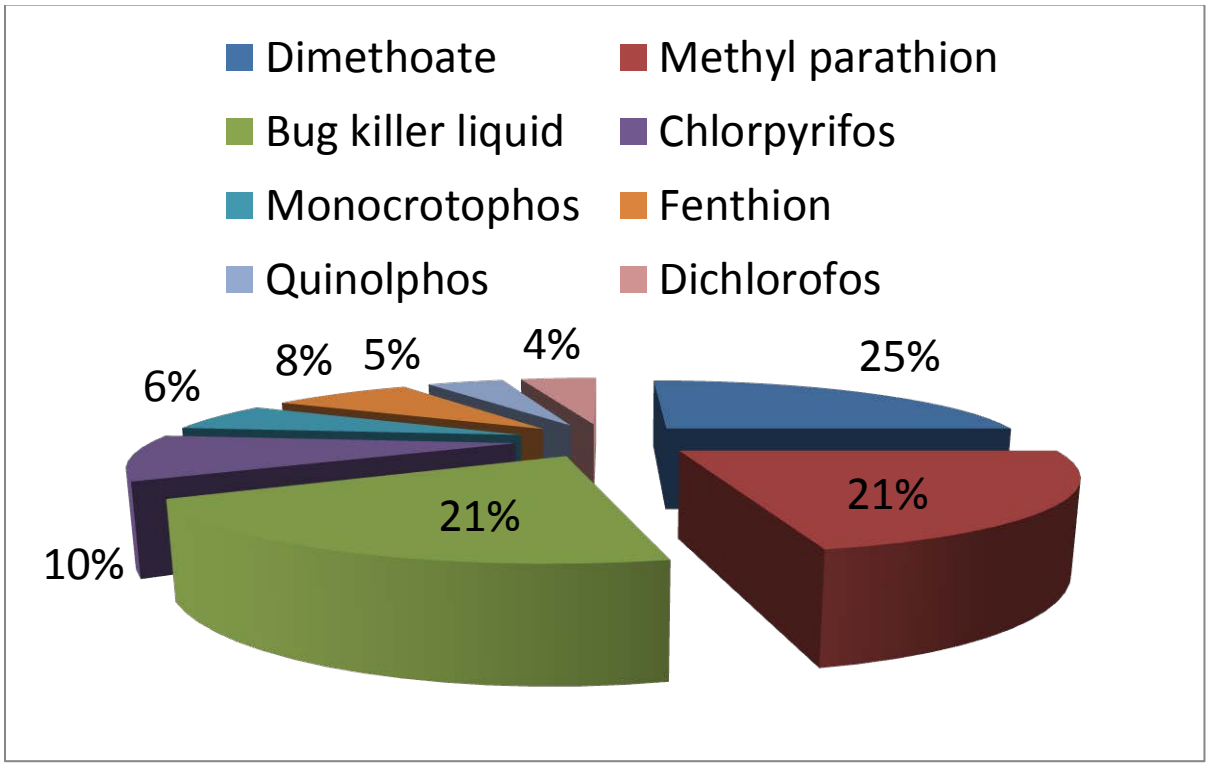


Table 4-OP agents consumed

Agents	DM	MP	BK	CP	MC	FN	QP	DC
No of patients	28	24	23	11	7	9	5	5

Figure 5-Time Interval from intake to admission and severity

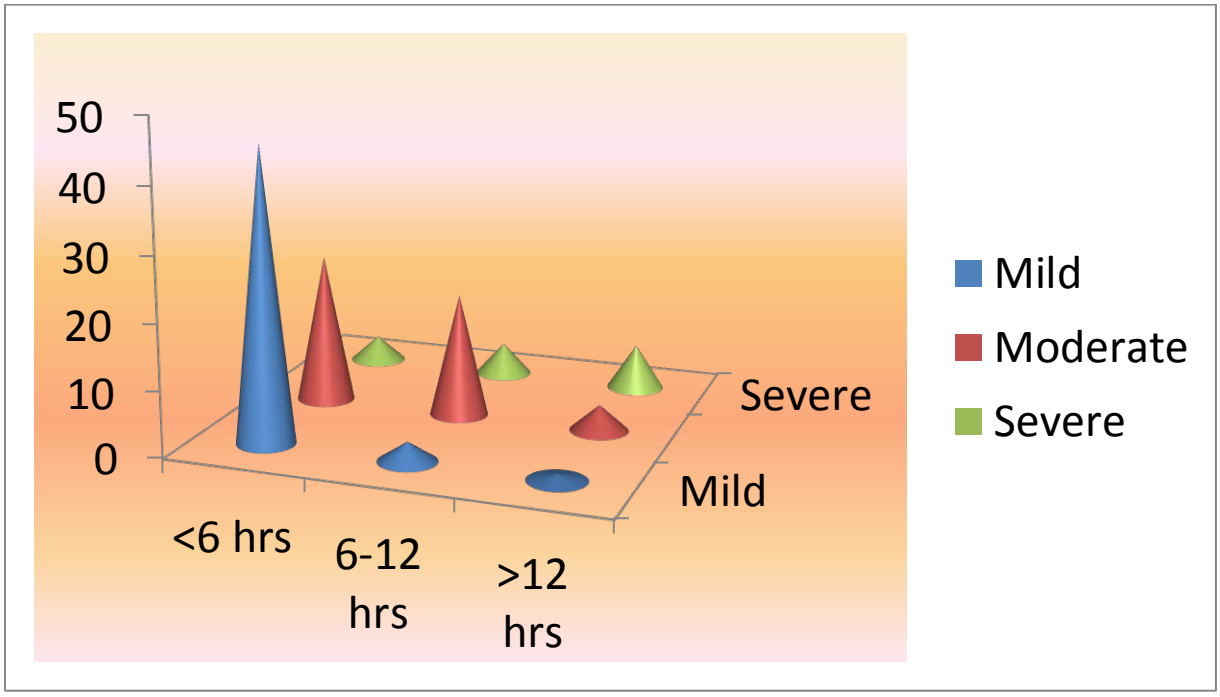


Table 5-Time Interval from intake to admission and severity

	Mild	**Moderate**	**Severe**
<6 hrs	46	24	5
6-12 hrs	2	18	5
>12 hrs	1	4	7

Thus the severity of poisoning correlates with late presentation to the hospital

Figure 6-Grading of secretions

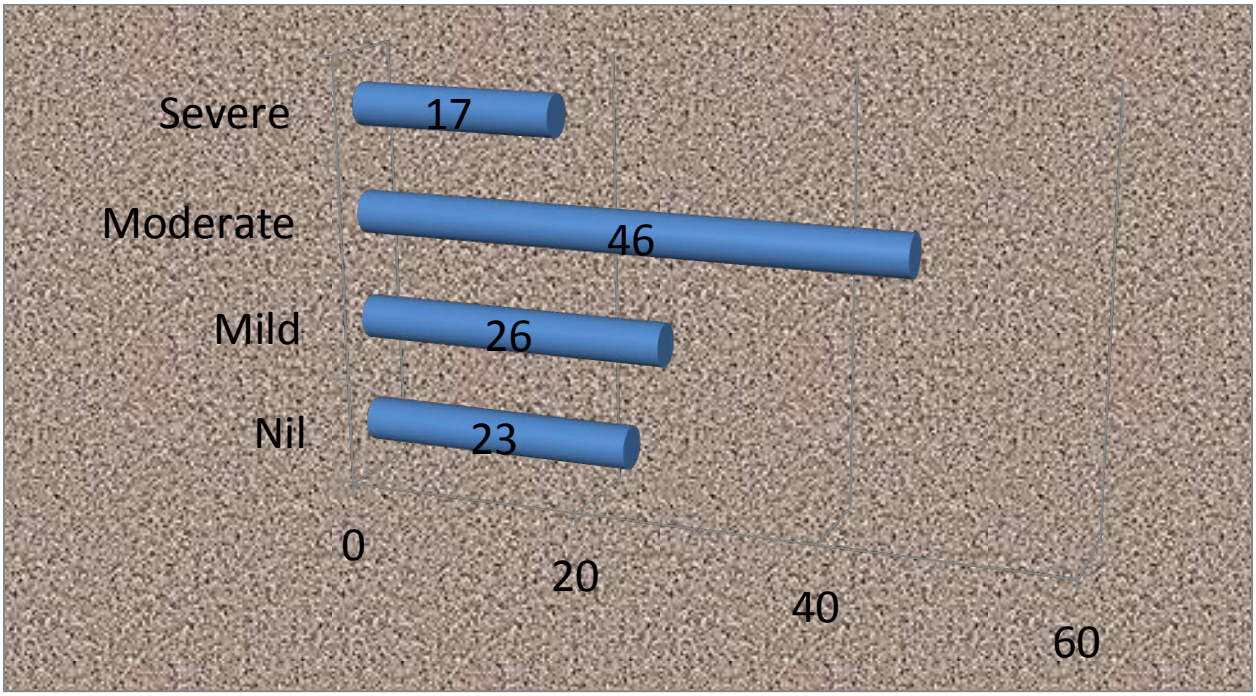


Figure 7- Exposure of poisoning

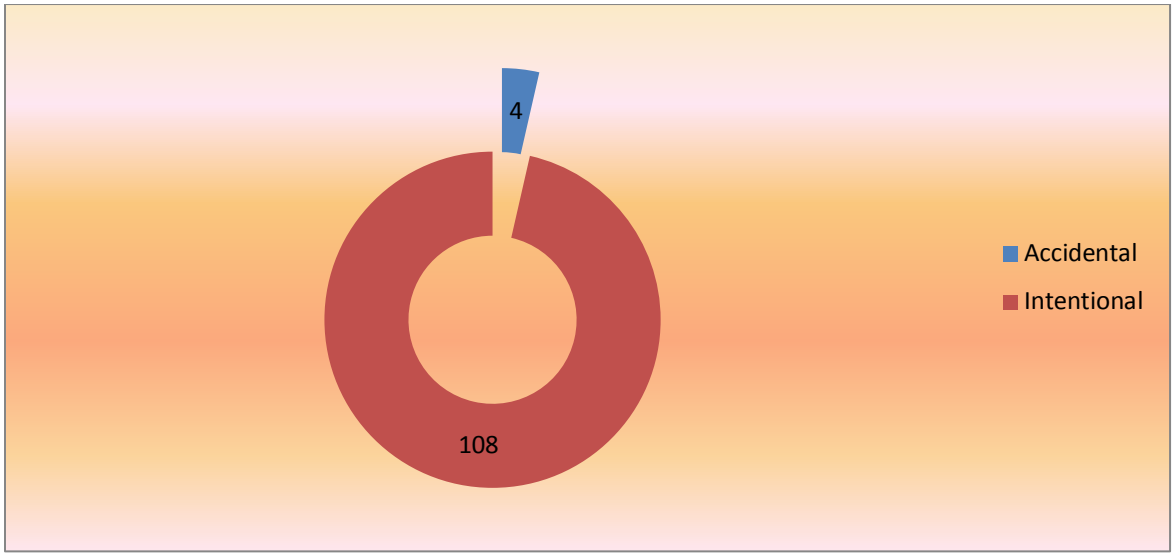


Figure 8-Clinical manifestations

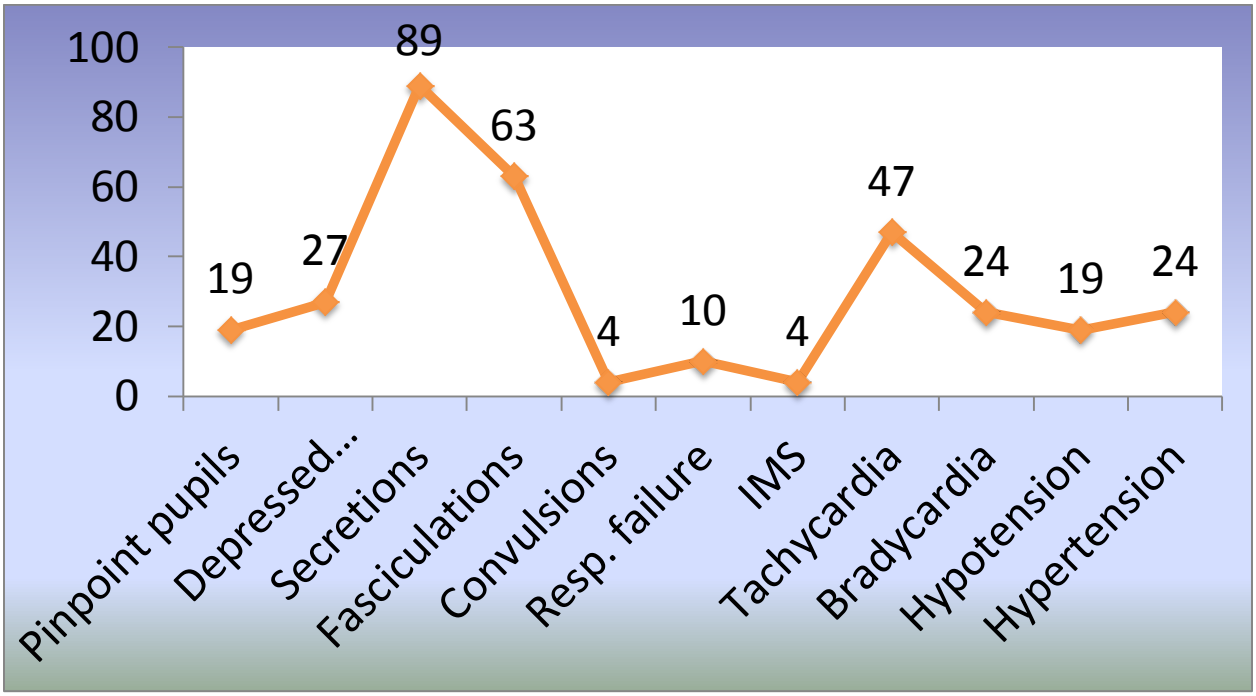


Table 6-Clinical manifestations

Clinical features	No of patients	Percentage of patients
Pin point pupils	19	16.9
Depressed mentation	27	24.1
Increased secretions	89	79.5
Fasciculations	63	56.25
Convulsions	4	3.57
Respiratory failure	10	8.93
IMS	4	3.57
Tachycardia	47	41.96
Bradycardia	24	21.43
Hypotension	19	16.96
Hypertension	24	21.43

Figure 9-Outcome

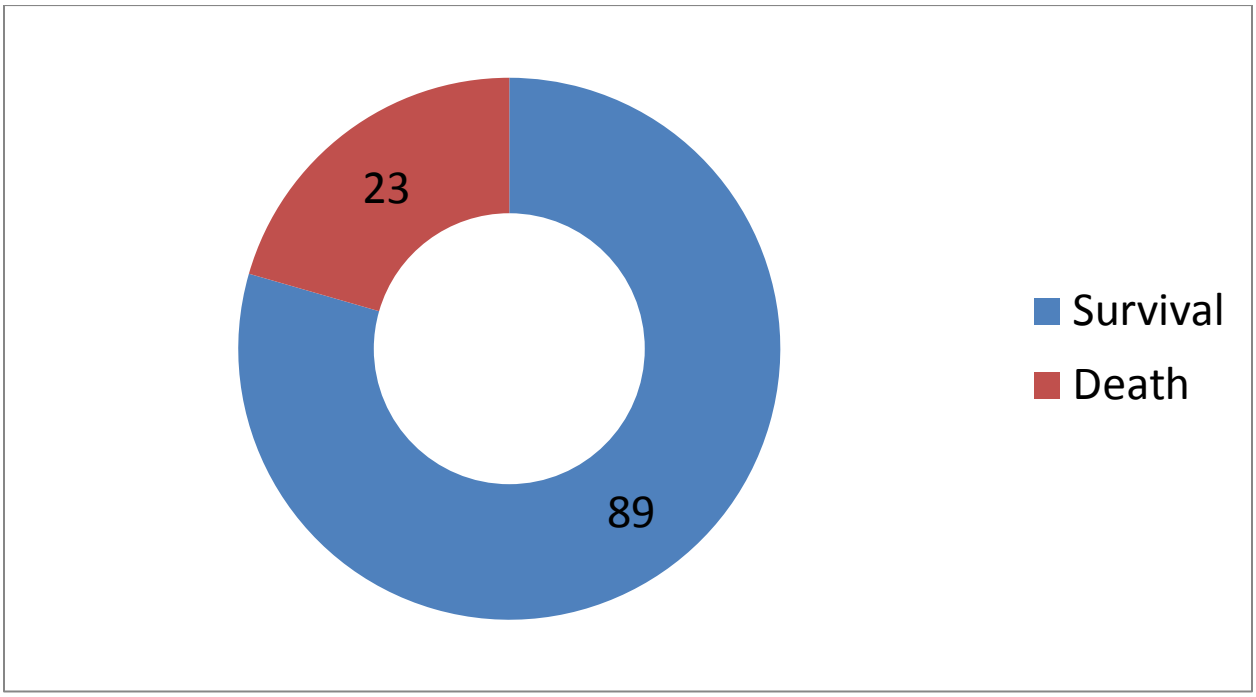


Figure 10 –Survival and death according to severity grading

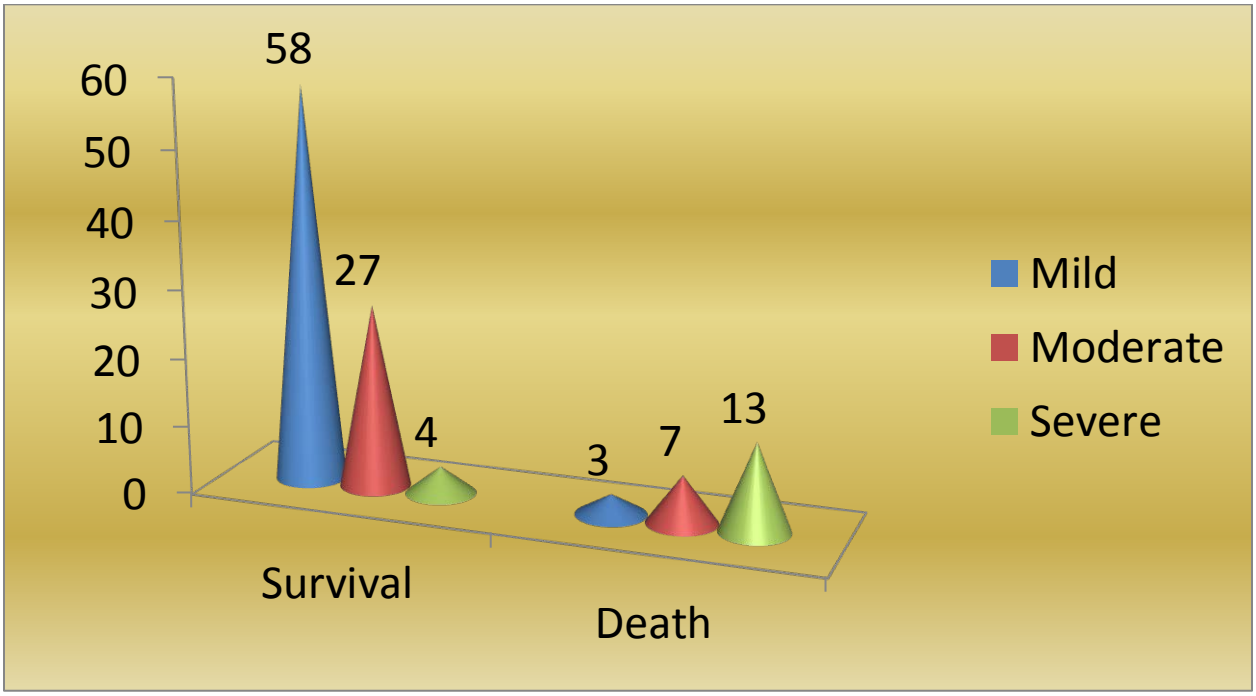


Figure 11-Patients categorized according to ECG changes and with severity grading

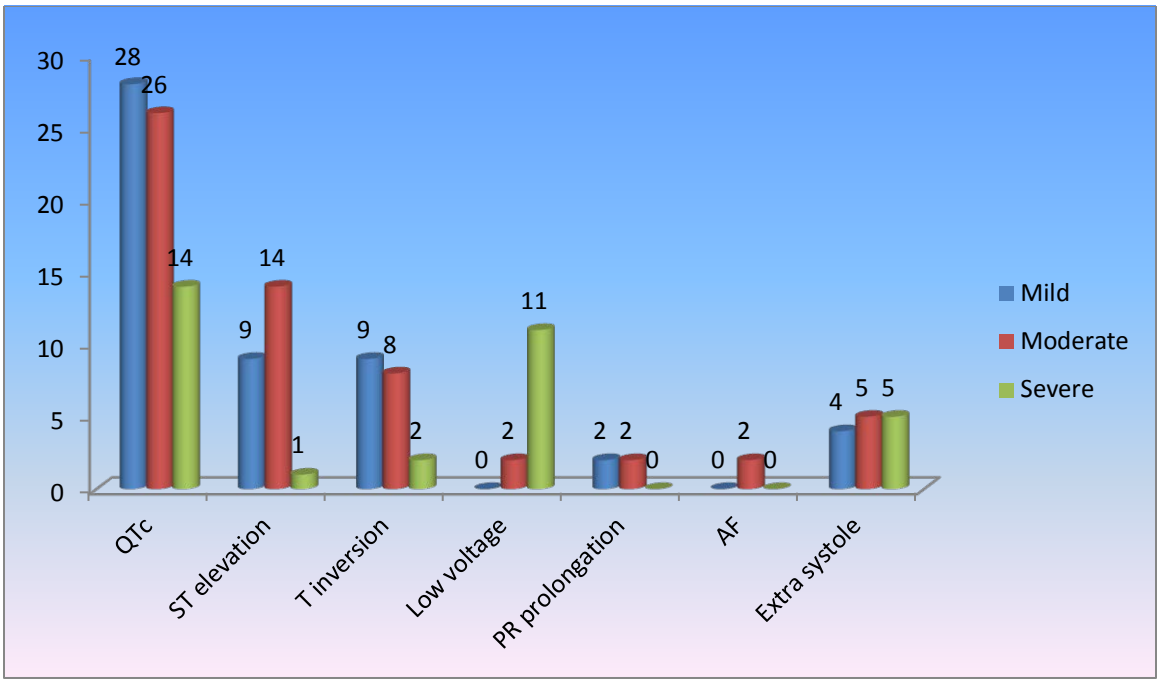


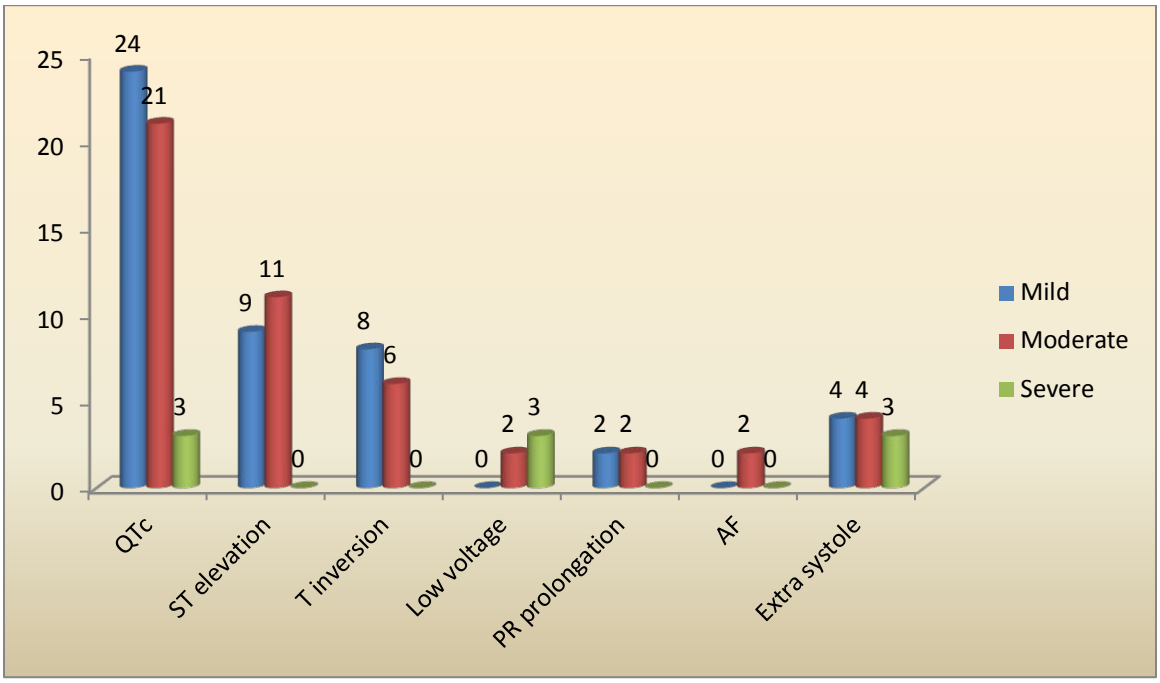
Table 7-Association of ECG changes with OP poisoning regarding their number of days of occurrence in serial 12 hour recordings

	MILD		MODERATE		SEVERE		P Value	Significance
	Mean (days)	SD	Mean (days)	SD	Mean (days)	SD		
QTc	2.39	0.92	1.88	0.77	1.28	0.95	**0.001**	Highly significant
ST elevation	1.22	0.26	0.82	0.32	0.50	0.00	**0.008**	Highly significant
T inversion	2.22	0.67	1.81	0.53	0.75	0.35	**0.019**	Significant
Low voltage	-	-	1.75	0.35	1.41	0.99	**0.651**	Not significant
PR prolongation	2.00	0.00	2.50	0.71	-	-	**0.424**	Not significant
AF	-	-	2.25	1.06	-	-	**-**	Not significant
Extra systole	0.87	0.25	1.60	0.55	0.81	0.27	**0.016**	Significant

This observation states that the association of QTc prolongation and ST elevation with OP poisoning with regard to the number of days of their occurrence in serial

12 hour ECGs appears to be highly significant; for T inversion and Extrasystole appears significant; and for Low voltage complexes, PR prolongation and AF appears not significant.

Figure 12-Survivors categorized according to ECG changes and with severity grading



The following table states that the association of QTc prolongation, T inversion and Extrasystole with OP poisoning with regard to the number of days of their hospital stay appears to be highly significant; for Low voltage complexes appears significant; and for ST elevation, PR prolongation and AF appears not significant.

Table 8-Association of ECG changes with Survivors regarding their number of days of hospital stay

	MILD		MODERATE		SEVERE		P Value	Significance
	Mean (days)	SD	Mean (days)	SD	Mean (days)	SD		
QTc	4.92	0.76	5.33	0.53	6.33	0.58	**0.002**	Highly significant
ST elevation	4.17	0.97	4.50	0.50	-	-	**0.338**	Not significant
T inversion	3.75	0.27	5.08	0.73	-	-	**<0.001**	Highly significant
Low voltage	-	-	5.00	0.00	6.66	0.58	**0.031**	Significant
PR prolongation	4.00	0.00	5.00	1.41	-	-	**0.422**	Not significant
AF	-	-	4.00	0.00	-	-	**-**	Not significant
Extra systole	4.125	0.63	4.62	0.48	6.33	0.58	**0.002**	Highly significant

Figure 13-Deceased patients categorized according to ECG changes and with severity grading

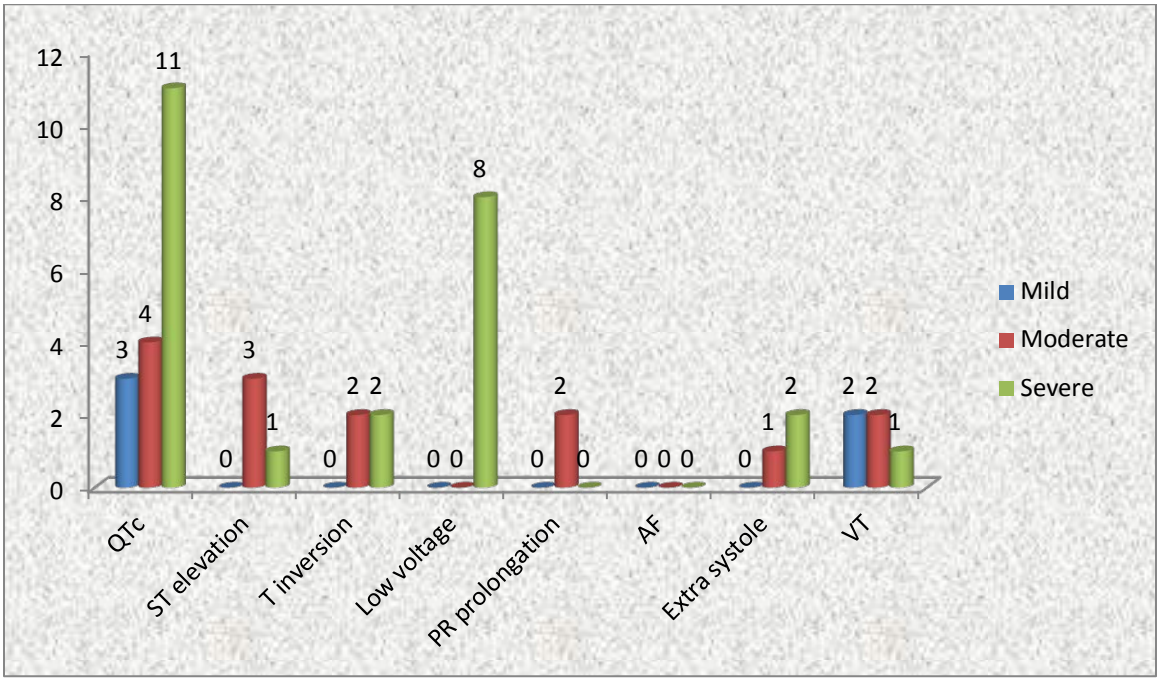


Table 9-Association of ECG changes with dead patients regarding their number of days of hospital stay

	MILD		MODERATE		SEVERE		P Value	Significance
	Mean (days)	SD	Mean (days)	SD	Mean (days)	SD		
QTc	3.83	0.76	1.75	0.50	1.14	0.45	**<0.001**	Highly significant
ST elevation	-	-	1.33	0.58	1.50	1.14	**0.823**	Not significant
T inversion	-	-	4.00	4.24	0.75	0.35	**0.393**	Not significant
Low voltage	-	-	1.50	0.41	0.875	0.44	**0.039**	Significant
PR prolongation	-	-	-	-	-	-	**-**	Not significant
AF	-	-	-	-	-	-	**-**	Not significant
Extra systole	-	-	7.00	0.00	0.75	0.35	**0.04**	Significant
VT	3.50	0.75	2.00	0.00	1.00	0.32	**<0.001**	Highly significant

This observation states that the association of QTc prolongation and Ventricular tachycardia with deceased OP poisoning patients with regard to the number of days of their hospital stay appears to be highly significant; for Low voltage complexes and Extrasystole appears significant; and for ST elevation, T inversion, PR prolongation and AF appears not significant.

Figure 14-Mean dose of atropine and P2AM with severity grading

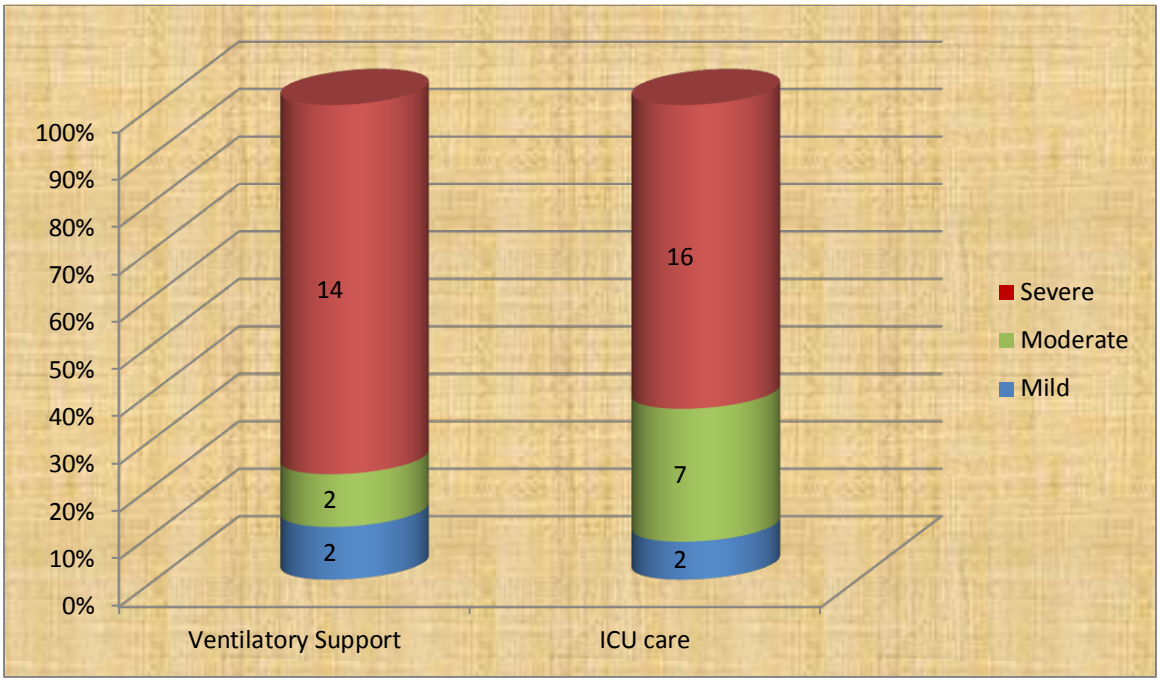


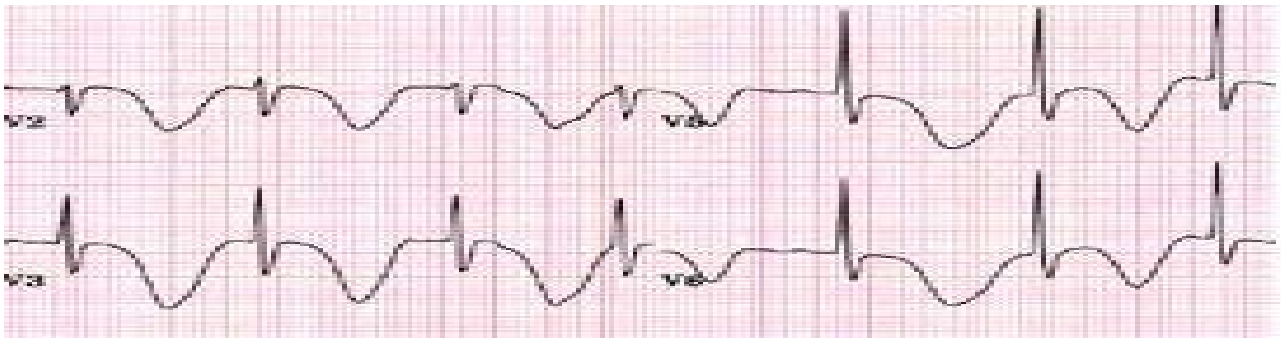
Table 10-Mean dose of atropine and P2AM with severity grading

Severity grading	Atropine treatment		P2AM treatment	
	Mean total dose (mg)	Mean days	Mean dose (g/day)	Mean days
Mild	46.82 ± 4.78	4.67±0.24	3.32 ±0.13	4.58±0.19
Moderate	80.56 ± 2.76	5.39 ± 0.37	4.23 ± 0.13	5.24 ± 0.44
Severe	138.41 ± 22.14	6.03 ± 0.54	5.76 ± 0.23	4.70 ± 0.42
Total	88.59 ± 8.45	5.33 ± 0.43	4.43 ± 0.18	4.84 ± 0.34

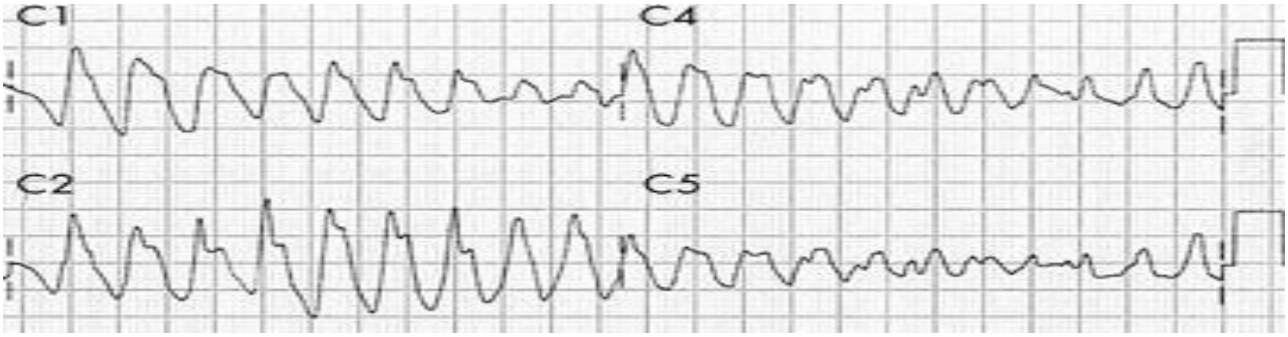
Atropine and Pralidoxime are the key treatment for OP poisoning. It is evident that the mean atropine and P2AM dose and the duration of treatment increase with increase in severity.

6.INTERESTING ECGS OBSERVED DURING THE STUDY

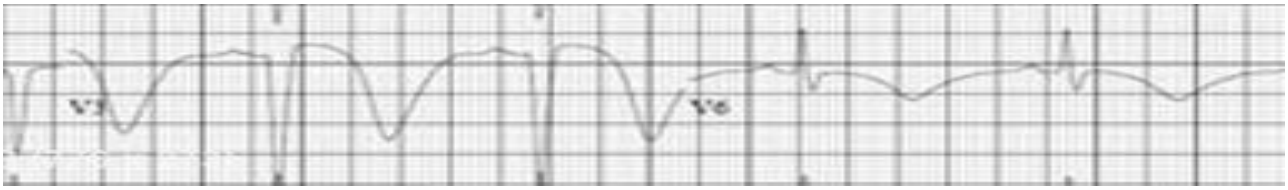
ECG of a severe grade poison case with low voltage complexes



A case of QT prolongation with giant T inversion who died on the 5th day



A case developing torsades de pointes following QT prolongation who survived with defibrillation



Another moderate severity case with QT prolongation who has died on the 4th day

7.DISCUSSION

Organophosphates and carbamates are frequently used pesticides which can lead to life threatening intoxication. Well over 50,000 organophosphate compounds have been synthesized since the first one by Clermont in 1857. All these compounds act by irreversible inhibition of acetylcholinesterase (Ach). The clinical symptoms range from classical cholinergic syndrome to flaccid paralysis and intractable seizures. About 99% of fatal poisoning occurs in developing countries particularly among farm workers. Despite an increased incidence of organophosphorus poisoning, the exact micromolecular changes that take place remain elusive. Till date atropine and oxime therapy continue to occupy the prime position in the specific management of OP poisoning.

Acute Organophosphorous compound poisoning is one of the most frequent poisonings encountered in Government Rajaji Hospital, Madurai. With the ease of availability and uncontrolled marketing, suicide has become the commonest mode of poisoning in developing countries.[7, 11]. The major cause of poisoning in our present study was attempted suicides (96.43%). In contrast, figures from developed countries like Japan, show accidental exposure forms a major bulk of organophosphorous compound poisoning cases.[9, 17] This rate was also consistent with the findings of Mahadi Balali Mood[114] et al about 94.3%

whereas it was reported to be 67% by AM Saadeh et al[86]. The accidental exposure in our study is only about 3.57%.

Age, Gender Prevalence

The vast majority of poisonings follow oral ingestion of liquid form and for almost all the patients gastric lavage was immediately done. In our study, the incidence was higher (32.14%) in the age group of 21-30 followed by 30.35% in the age group of 31-40. These are consistent with the findings of Muhammet Guven et al[115], S Singh et al[68] and AM Saadeh et al[86] where the mean values were 24.1, 23.25 and 23.95 respectively.

In the present study, 79% of the patients were males. This correlates with the findings of the previous studies. However, in a study done by M. Vishwanathan et al[69], 66% of the patients who consumed organophosphorous compound were females.

Dimethoate (Rogar) accounted for about 25% of intoxication followed by methyl parathion and bug killer liquid of 21% each respectively. The commonest mode of intake was found to be poison along with alcohol about 47% followed by poison with water about 27%. Of the 49 mild cases, 46 fell under early admission within 6 hours of intake whereas of the 12 severe cases about 7 fell under late

presentation of more than 12 hours establishing a direct correlation of severity with time delay.

Both the present study and that of Mahdi Balali-Mood et al, found association between the severity of poisoning and clinical manifestations. The most marked muscarinic signs in our study group were, increased secretions (79.5%), pin point pupils (16.9%) and respiratory failure (8.93%). In studies done by OP Gupta et al[70], Sarjit Singh et al[71], and, Goel et al[64] vomiting was present in 90% and 97.08% of the cases respectively due to chemical gastritis. The most prominent of the nicotinic effect of our study is muscular end plate block, resulting in muscle weakness and fasciculations (56.25%), tachycardia (41.96%), bradycardia (21.43%), hypotension (16.96%), hypertension (21.43%). The CNS symptoms like depressed mentation (24.1%) and convulsions (3.57%) were also present. In comparison, studies done by Goel et al[64] and Sarjit Singh et al[71] showed that 55% and 100% of the patients respectively had fasciculations. In a study done by Robert et al[72] 19% of the patients had bradycardia, while in a study carried out by Semir Nouria[73], 17% had bradycardia.

About 14 (77.77%) of 18 and 16 (64%) of 25 patients of ventilator support and ICU care respectively belong to the severe grade of poisoning establishing their direct association with each other. The mean atropine and P2AM dose and the

duration of treatment increase with increase in severity of poisoning as observed with most of the reference studies.

The outcome of study was that 20.53% of patients (23 of 112) died and 79.46% survived (89 of 112). Though 76.46% patients survived, about 65.16% of survivors fell under mild grading whereas though total deaths was only 20.53%, about 56.52% of deceased fell under severe grading.

Among the ECG changes observed overall, QTc prolongation tops the list with 68 cases(60.7%) followed by ST elevation (21.4%), T inversion(16.9%), Extra systole(12.5%), Low voltage complexes(11.6%), PR prolongation(3.5%) and AF(1.7%) with 24,19,14,13,4 and 2 cases respectively. This is similar to that observed by A M Saadeh et al, P. Karki et al, Yurumez et al, Chuang et al, Kiss and Fazekas[44] and Manojith Mookherjee. The association of QTc prolongation and ST elevation with OP poisoning with regard to the number of days of their occurrence in serial 12 hour ECGs appears to be highly significant; for T inversion and Extrasystole appears significant; and for Low voltage complexes, PR prolongation and AF appears not significant.

Among the ECG changes of survivors, QTc prolongation tops the list with 48 cases followed by ST elevation, T inversion, Extra systole, Low voltage complexes, PR prolongation and AF with 20,14,11,5,4 and 2 cases respectively.

Thus the association of QTc prolongation ,T inversion and Extrasystole with OP poisoning with regard to the number of days of their hospital stay appears to be highly significant; for Low voltage complexes appears significant; and for ST elevation, PR prolongation and AF appears not significant. This is consistent with that of Rousseau JM.[66]

Among the patients who died, QTc prolongation tops the list with 18 cases followed by Low voltage complexes, Ventricular tachycardia, ST elevation, T inversion, Extra systole, , PR prolongation and AF with 8,5,4,4,3,2 and 0 cases respectively as observed Dalvi, Karki, Yemasheta M[67] and A M Saadeh et al.Thus the association of QTc prolongation and Ventricular tachycardia with dead OP poisoning patients with regard to the number of days of their hospital stay appears to be highly significant; for Low voltage complexes and Extrasystole appears significant; and for ST elevation, T inversion, PR prolongation and AF appears not significant.

8.CONCLUSION

In India, organophosphorus compounds cause more suicidal deaths among the earning and nonearning members of the society. This study was carried out with an aim to establish the correlation of ECG changes with prognosis in OP poisoning. This was a cross sectional study that involved 112 OP poison cases that fit the criteria for our study. From all the observations and discussions made so far, we can conclude that

1) The clinical features well reflected the severity of the poisoning. Patients presenting later than 6 hours manifested more severity.
2) The mean atropine and pralidoxime dosage needed appears to increase as the severity increases.
3) More than half of the death cases fell under severe category
4) ECG changes most commonly encountered were QTc prolongation (60.7%) followed by ST elevation (21.4%), T inversion(16.9%), Extra systole(12.5%), Low voltage complexes(11.6%), PR prolongation(3.5%) and AF(1.7%).
5) By statistical values, QTc prolongation, ST elevation, T inversion and Extrasystole were significantly associated with OP poisoning. Among survivors, QTc prolongation, T inversion, low voltage complexes and

Extrasystole were significantly associated with the prolonged duration of hospital stay. Among the death cases, QTc prolongation, Ventricular tachycardia, low voltage complexes and Extrasystole were significantly associated.

6) Despite improvement in clinical features, ECG changes particularly QTc prolongation has got independent prognostic values as evidenced in some cases with good clinical recovery but with prolonged QTc interval suffered sudden cardiac death as a result of torsades de pointes VT.

Thus we conclude from this study that Electrocardiographic changes correlated independently with the prognosis of the OP poisoning cases and the identification of them, particularly QTc prolongation and timely shifting of cases to ICU and CCU where adequate resuscitative measures, ventricular pacing facilities available can prevent such sudden cardiac deaths. Blood transfusion is said to have a role in severe poisoning in rapidly replenishing acetylcholinesterase enzyme. Intensive supportive care, meticulous respiratory care and administration of atropine in adequate dosage very early in the course of treatment are also emphasized.

9.LIMITATIONS OF THE STUDY

- Routine biochemical recordings including serum electrolytes which can influence ECG changes were not observed.
- Due to non availability, serum or RBC cholinesterase levels cannot be analyzed in grading the severity of poisoning.
- Chest roentgenography findings like non-cardiogenic pulmonary edema were not included in severity grading.
- Echocardiogram not included in the study.

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PROFORMA

CORRELATION OF ELECTROCARDIOGRAPHIC CHANGES WITH PROGNOSIS IN ORGANOPHOSPHORUS POISONING

PARTICULARS OF THE PATIENT: Case No:

Name : Hospital No.
Age :
Sex :
Address:
Date of Admission:
Date of discharge:
Suicide/accidental
Final Diagnosis:

COMPLAINTS WITH DURATION

- Time and date of consumption of Organophosphorous compound poison :
- Time between poisoning and admission:
- Compound name: Trade name :
- Quantity consumed
- Mode of consumption:
- Inhalation / Ingestion / Injection
- Vomiting/ diarrhoea
- Altered sensorium
- Hyper salivation
- Convulsion
- Other Complaints
- Referred from :

Family History:
Past History:
Personal History:

On Examination:

Build
Nourishment
Wasting
Pallor Cyanosis Icterus

Lymphadenopathy Clubbing Edema

Pulse: Breath Smell:
B.P: Tongue:
R.R.: Skin:
Temperature:
C.N.S
Sensorium: Normal / Restlessness / Drowsiness/Coma
GCS: V E M =
Pupils:
Fasciculations: Total score
Weakness
Proximal muscle
Neck muscle
Respiratory muscle:
a) Single breath count:
b) Accessory muscle:

P.A:
R.S:
C.V.S:

DIAGNOSIS:
Mild Poisoning / Moderate Poisoning / Severe Poisoning

ECG interpretation (hours after admission)

	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Rate											
Rhythm											
Low voltage											
P wave											
PR interval											
QRS width											
ST segment											
QT segment											
Corrected QT											
T wave											
Extrasystole											
VT											

Management:

Body wash:

Stomach wash:

	Dose within the first 48 hrs	Dose after 48 hrs of admission
Atropine:		
P2AM :		
Fluids:		
Others:		

Intubation's Hour after the consumption of O.P. Poisoning :

Ventilation:

Those who developed intermediate syndrome:

Those who developed complication Pneumonia

Pneumothorax:

ICU Stay (Hrs) :

Hospital Stay (Hrs) :

OUTCOME : RECOVERED EXPIRED

MASTER CHART

SL. NO	Age	Sex	Type of exposure	Agents	Mode of consumption	Time interval (consumption to admission) in hours	Pulse rate per min	BP (mm Hg)	Clinical features						
									P	M	S	F	C	RF	IMS
1	44	Male	IE	MP	PA	3	51	130/90	-	-	+	-	-	-	-
2	32	Male	IE	BK	PA	3.5	88	126/80	-	+	++	+	-	-	-
3	24	Male	IE	MP	PW	5.5	108	112/78	-	-	+	-	-	-	-
4	23	Male	IE	DM	PA	8	111	110/70	-	-	+	-	-	-	-
5	35	Female	IE	DM	Ot	2.25	87	100/70	-	-	-	-	-	-	-
6	38	Male	IE	DC	PA	2.25	91	150/100	-	-	++	+	-	-	-
7	27	Male	IE	MP	PA	1.25	94	120/80	-	-	-	-	-	-	-
8	57	Female	IE	MP	PW	7	118	90/60	-	-	++	+	-	-	-
9	36	Male	IE	QP	PA	5	84	100/70	-	-	+	-	-	-	-
10	47	Male	IE	DM	PA	14.25	122	80/50	+	+	+++	+	-	+	-
11	22	Male	IE	MP	PW	2.5	82	108/70	-	-	-	-	-	-	-
12	61	Male	AE	BK	PA	3	58	152/98	+	+	+++	+	+	-	-
13	33	Male	IE	FN	PA	3.75	77	130/90	-	-	+	-	-	-	-
14	61	Male	IE	DM	PA	8.25	132	90/60	-	+	++	+	-	-	-
15	29	Female	IE	MP	AL	5.5	71	122/80	-	-	+	-	-	-	-
16	20	Male	IE	BK	PW	8	106	116/78	-	-	++	+	-	-	-
17	19	Male	IE	DM	PA	6	90	120/82	-	-	+	-	-	+	+
18	31	Male	IE	MP	PA	7.25	102	110/70	-	-	++	+	-	-	-
19	36	Male	IE	CP	PW	3.5	51	148/98	-	-	-	-	-	-	-
20	25	Female	IE	DC	PM	3.75	112	112/70	-	-	++	+	-	-	+
21	27	Male	IE	DM	PA	7.5	121	80/50	+	+	+++	+	-	+	-
22	17	Male	IE	MP	PA	2.5	75	120/90	-	-	+	-	-	-	-
23	20	Male	IE	BK	PA	5.5	68	100/70	-	+	++	+	-	-	-
24	44	Female	AE	FN	Ot	9	53	140/100	-	-	+	-	-	-	-
25	36	Male	IE	DM	PW	3.5	73	120/80	-	+	++	+	-	-	-
26	39	Male	IE	MP	PW	3.25	118	128/90	-	-	++	+	-	-	-
27	50	Male	IE	BK	PA	2.5	123	90/50	+	+	+++	+	-	-	-

MASTER CHART

SL. NO	Age	Sex	Type of exposure	Agents	Mode of consumption	Time interval (consumption to admission) in hours	Pulse rate per min	BP (mm Hg)	Clinical features						
									P	M	S	F	C	RF	IMS
28	59	Male	IE	CP	PA	1.75	49	150/90	-	-	-	-	-	-	-
29	23	Male	IE	DM	PA	6.5	87	110/80	-	+	++	+	-	-	-
30	18	Male	IE	BK	PM	4	81	120/88	-	-	+	-	-	-	-
31	29	Male	IE	FN	PW	8	125	122/80	-	+	++	+	-	-	-
32	27	Female	IE	DM	AL	14	79	110/70	-	-	++	+	-	-	-
33	41	Male	IE	BK	PW	13	113	70/40	+	+	+++	+	-	+	-
34	39	Male	IE	DM	PA	3.5	55	150/90	-	-	+	-	-	-	-
35	34	Male	IE	MP	PA	3	107	102/78	-	-	++	+	-	-	-
36	19	Male	IE	DM	PA	9.5	66	100/70	-	+	++	+	-	-	-
37	27	Female	IE	MC	AL	2.5	69	120/80	-	-	+	-	-	-	-
38	29	Male	IE	FN	PW	8	109	90/60	+	+	++	+	-	-	-
39	32	Male	AE	DM	PW	5	89	110/80	-	-	+	-	-	-	-
40	37	Female	IE	BK	PM	5.5	112	122/84	-	-	++	+	-	-	-
41	47	Female	IE	MP	PW	6.5	51	160/100	+	+	+++	+	+	-	-
42	51	Male	IE	DM	PA	4.5	57	164/90	-	-	++	+	-	-	-
43	17	Male	IE	QP	PA	11	115	124/82	-	-	++	+	-	-	-
44	28	Male	IE	BK	PA	2.5	91	134/82	-	-	+	-	-	-	-
45	33	Female	IE	DM	AL	8	106	80/40	+	+	+++	+	-	+	-
46	15	Male	IE	MP	PW	1	76	100/70	-	-	+		-	-	-
47	29	Male	IE	MC	AL	0.75	89	110/80	-	-	-	-	-	-	-
48	34	Male	IE	BK	PA	8.75	114	122/84	-	-	++	+	-	-	-
49	37	Male	IE	DM	PA	1.5	53	130/90	-	-	+	-	-	-	-
50	45	Male	IE	MP	PA	16	59	156/102	-	-	++	+	-	-	-
51	54	Female	IE	DC	PM	4	45	160/90	-	-	-	-	-	-	-
52	26	Male	IE	BK	PW	16	134	78/52	+	+	+++	+	+	-	-
53	30	Female	IE	DM	PW	5.25	75	120/84	-	-	++	+	-	-	-
54	39	Male	IE	MP	AL	2.25	93	100/70	-	-	-	-	-	-	-
55	24	Female	IE	CP	PW	4.5	87	110/80	-	-	-	-	-	-	-

MASTER CHART

SL. NO	Age	Sex	Type of exposure	Agents	Mode of consumption	Time interval (consumption to admission) in hours	Pulse rate per min	BP (mm Hg)	Clinical features						
									P	M	S	F	C	RF	IMS
56	21	Male	IE	BK	PA	4.5	118	104/80	-	-	++	+	-	-	-
57	52	Male	IE	DM	PA	3.5	48	160/100	-	-	+	-	-	-	-
58	19	Male	IE	MP	PA	5	133	100/78	-	-	++	+	-	-	-
59	22	Male	IE	BK	AL	7	90	120/80	-	-	++	+	-	-	-
60	27	Male	IE	FN	AL	7.5	104	128/82	-	-	++	+	-	-	-
61	37	Male	IE	DM	PW	7	142	84/56	+	+	+++	+	-	+	-
62	39	Female	IE	MP	PW	2	95	110/70	-	-	++	+	-	-	-
63	63	Male	IE	QP	AL	1.5	50	166/98	-	-	+	-	-	-	-
64	46	Male	IE	BK	PA	2.5	45	152/90	-	-	+	-	-	-	-
65	17	Male	IE	MP	PA	11.5	78	120/90	-	-	++	+	-	-	-
66	49	Male	IE	CP	PA	7	?	??	+	+	+++	+	-	+	-
67	33	Female	IE	MC	AL	4.5	82	134/90	-	-	-	-	-	-	-
68	15	Male	IE	FN	PW	3	90	128/80	-	-	++	+	-	-	-
69	28	Male	IE	MP	PA	7.5	55	110/80	-	-	++	+	-	-	-
70	32	Male	IE	MC	PA	2	51	148/100	-	-	-	-	-	-	-
71	38	Male	IE	MP	PA	3,5	141	92/58	+	+	+++	+	-	-	-
72	61	Male	IE	DM	AL	10	76	100/70	+	-	++	+	-	-	+
73	49	Female	IE	FN	AL	4.5	48	154/98	-	-	+	-	-	-	-
74	55	Male	IE	BK	PW	3	75	150/90	-	-	-	-	-	-	-
75	24	Male	IE	DM	PW	2.5	80	120/80	-	-	++	+	-	-	-
76	29	Female	IE	CP	AL	5.5	53	150/88	+	+	+++	+	-	-	-
77	30	Male	IE	MC	PA	4	79	130/90	-	-	+	-	-	-	-
78	44	Male	IE	MP	PA	4.5	148	88/52	+	+	+++	+	-	-	-
79	61	Male	IE	DM	PA	13	87	100/60	-	-	-	-	-	-	-
80	30	Female	IE	FN	AL	8.25	114	110/82	-	-	++	+	-	-	-
81	39	Male	IE	BK	PW	13	81	90/60	-	-	++	+	-	-	-
82	31	Male	IE	CP	PW	2.5	70	120/80	-	-	-	-	-	-	-
83	22	Male	IE	MP	AL	4.5	73	130/90	-	-	-	-	-	-	+
84	27	Female	IE	CP	PM	4.5	112	128/82	-	-	++	+	-	-	-

MASTER CHART

SL. NO	Age	Sex	Type of exposure	Agents	Mode of consumption	Time interval (consumption to admission) in hours	Pulse rate per min	BP (mm Hg)	Clinical features						
									P	M	S	F	C	RF	IMS
85	19	Male	IE	DM	PW	1	85	100/72	-	-	-	-	-	-	-
86	41	Male	IE	CP	PA	5.5	128	94/58	-	+	++	+	-	-	-
87	58	Male	IE	MP	PA	2.75	56	156/100	-	-	+	-	-	-	-
88	49	Male	IE	BK	PA	14	?	??	+	+	+++	+	+	+	-
89	26	Female	IE	DM	AL	1.5	121	118/88	-	-	++	+	-	-	-
90	19	Male	IE	QP	PW	2	83	102/70	-	-	-	-	-	-	-
91	30	Female	IE	BK	AL	4	90	110/70	-	-	++	+	-	-	-
92	37	Male	IE	DM	PW	4	56	150/98	-	-	-	-	-	-	-
93	32	Male	IE	CP	PA	3	65	130/90	-	-	-	-	-	-	-
94	50	Male	IE	BK	PA	12.5	120	70/40	+	+	+++	+	-	-	-
95	26	Male	IE	DC	PA	4.75	74	120/80	-	-	+	-	-	-	-
96	29	Male	IE	MP	PA	5	89	110/80	-	-	+	-	-	-	-
97	31	Male	IE	MC	PA	7	114	112/78	-	-	++	+	-	-	-
98	37	Male	IE	FN	AL	3.5	76	148/96	-	-	++	+	-	-	-
99	33	Female	IE	DM	PW	15	135	70/42	+	+	+++	+	-	+	-
100	40	Male	IE	BK	PA	5.25	85	118/80	-	-	++	+	-	-	-
101	22	Male	IE	CP	PA	2.5	69	100/74	-	-	+	-	-	-	-
102	49	Male	IE	DC	PA	3.5	49	160/90	-	-	-	-	-	-	-
103	28	Female	AE	BK	AL	8	114	118/70	-	-	++	+	-	-	-
104	22	Male	IE	DM	PW	2	88	122/88	-	-	-	-	-	-	-
105	18	Male	IE	MC	PM	1.75	84	100/70	-	-	-	-	-	-	-
106	46	Male	IE	BK	AL	13.5	165	60/?	+	+	+++	+	-	+	-
107	62	Male	IE	DM	PW	3	51	160/90	-	-	+	-	-	-	-
108	37	Male	IE	CP	AL	2	121	100/72	-	-	++	+	-	-	-
109	31	Male	IE	MP	PA	9.5	59	156/92	-	-	++	+	-	-	-
110	29	Male	IE	QP	PA	5.5	90	110/80	-	+	++	+	-	-	-
111	23	Male	IE	BK	PA	5.75	117	100/70	-	-	-	-	-	-	-
112	35	Female	IE	DM	PW	15	51	150/90	-	-	++	+	-	-	-

MASTER CHART

SL. NO	Low Voltage		ST elevation		Inverted T		Prolonged PR Interval		Atrial fibrillation		Extra systole		Ventricular tachycardia		QTc Prolongation		Treatment					
	A	N	A	N	A	N	A	N	A	N	A	N	A	N	A	N	At	Pr	V	ICU	HS	O
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	75	3	-	-	5	S
2	-	-	-	-	-	-	-	-	-	-	1	3	-	-	-	-	75	4	-	-	5	S
3	-	-	-	-	1	4.5	-	-	-	-	-	-	-	-	-	-	59	3	-	-	4	S
4	-	-	-	-	-	-	-	-	-	-	-	-	4	-	2	-	50	3	-	-	4	D
5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	4	39	3	-	-	6	S
6	-	-	0.5	1.5	-	-	-	-	-	-	-	-	-	-	-	-	85	4	-	-	4	S
7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	35	3	-	-	5	S
8	-	-	0.5	-	-	-	-	-	-	-	-	-	-	-	-	-	154	4	-	-	1	D
9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	4	40	3	-	-	6	S
10	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	125	5	0.5	0.5	1	D
11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	3	43	3	-	-	5	S
12	0	2.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	175	5.5	-	5	7	S
13	-	-	0.5	2	-	-	-	-	-	-	-	-	-	-	-	-	47	3	-	-	3.5	S
14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	-	100	4	-	1	2	D
15	-	-	-	-	0.5	4	-	-	-	-	-	-	-	-	-	-	54	3	-	-	3.5	S
16	-	-	-	-	-	-	1	3	-	-	-	-	-	-	-	-	75	4	-	-	4	S
17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	6	59	4	11	11	18	S
18	-	-	-	-	-	-	-	-	-	-	-	-	3	3	1	4	65	4	-	3	6	S
19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	46	4	-	-	6	S
20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	3	55	4	6	6	12	S
21	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	-	220	5	1	1	1.5	D
22	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	3	43	3	-	-	5	S
23	-	-	1	2	-	-	-	-	-	-	-	-	-	-	-	-	85	4	-	-	4	S
24	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	43	4	-	-	6	S
25	-	-	-	-	1	3	-	-	-	-	-	-	-	-	-	-	85	5.5	-	-	5	S
26	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	65	4	-	-	5	S
27	0	3	-	-	-	-	-	-	-	-	2	3	-	-	0	3	100	7	3.5	3.5	6	S

MASTER CHART

SL. NO	Low Voltage		ST elevation		Inverted T		Prolonged PR Interval		Atrial fibrillation		Extra systole		Ventricular tachycardia		QTc Prolongation		Treatment					
	A	N	A	N	A	N	A	N	A	N	A	N	A	N	A	N	At	Pr	V	ICU	HS	O
28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.5	4	37	4	-	-	7	S
29	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	2.5	78	5.5	-	-	5	S
30	-	-	-	-	1	2.5	-	-	-	-	-	-	-	-	-	-	50	3	-	-	4	S
31	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	3	68	4	-	-	5	S
32	-	-	-	-	-	-	-	-	-	-	2	4	-	-	-	-	60	4	-	-	5	S
33	0	-	-	-	-	-	-	-	-	-	0	-	-	-	0	-	144	5.5	0.5	0	0.5	D
34	-	-	0.5	1.5	-	-	-	-	-	-	-	-	-	-	-	-	47	3	-	-	4	S
35	0	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100	4	-	-	5	S
36	-	-	0.5	1.5	-	-	-	-	-	-	-	-	-	-	-	-	84	5.5	-	-	5	S
37	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3.5	46	3	-	-	6	S
38	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	-	135	4	-	0.5	1	D
39	-	-	-	-	-	-	-	-	-	-	1	2	-	-	-	-	37	3	-	-	4	S
40	-	-	-	-	1.5	2.5	-	-	-	-	-	-	-	-	0.5	3	84	5.5	-	-	5.5	S
41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	95	7	2	2	2	D
42	-	-	1	1.5	-	-	-	-	-	-	-	-	-	-	-	-	96	4	-	-	4	S
43	-	-	-	-	0	2.5	-	-	-	-	-	-	-	-	0.5	2.5	70	4.5	-	-	6	S
44		-	-	-	1	3	-	-	-	-	-	-	-	-	-	-	55	3	-	-	4	S
45	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	-	130	7	1	1	1.5	D
46	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	-	45	3	-	-	4.5	D
47	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	4	44	4	-	-	6	S
48	-	-	1	1.5	-	-	-	-	-	-	-	-	-	-	-	-	75	4.5	-	-	5	S
49	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	49	4	-	-	5	S
50	-	-	0	1	-	-	-	-	-	-	-	-	2	-	1	-	100	4	-	-	2	D
51	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	3.5	47	4	-	-	5	S
52	-	-	-	-	0	-	-	-	-	-	0	-	1	-	0	-	155	7	1	1	1	D
53	-	-	0.5	1	-	-	-	-	-	-	-	-	-	-	-	-	94	5.5	-	-	4	S
54	-	-	-	-	0.5	2.5	-	-	-	-	-	-	-	-	-	-	47	3	-	-	3.5	S
55	-	-	-	-	-	-	-	-	-	-	1.5	2	-	-	-	-	49	3	-	-	3.5	S

MASTER CHART

SL. NO	Low Voltage		ST elevation		Inverted T		Prolonged PR Interval		Atrial fibrillation		Extra systole		Ventricular tachycardia		QTc Prolongation		Treatment					
	A	N	A	N	A	N	A	N	A	N	A	N	A	N	A	N	At	Pr	V	ICU	HS	O
56	-	-	-	-	-	-	-	-	1	4	-	-	-	-	-	-	90	4	-	-	4	S
57	-	-	0	1	-	-	-	-	-	-	-	-	-	-	-	-	53	3	-	-	4	S
58	0	1.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	110	4	-	-	5	S
59	-	-	-	-	0.5	2.5	-	-	-	-	-	-	-	-	0.5	2.5	74	4.5	-	-	4.5	S
60	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	2.5	65	4	-	-	5	S
61	-	-	-	-	-	-	-	-	-	-	-	-	1	-	0	-	132	7	1	1	1	D
62	-	-	1	2	-	-	-	-	-	-	-	-	-	-	1	2	70	4	-	-	5	S
63	-	-	0	1.5	-	-	-	-	-	-	-	-	-	-	2	4.5	49	4	-	-	6	S
64	-	-	-	-	-	-	1	3	-	-	-	-	-	-	-	-	55	3	-	-	4	S
65	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	2	75	4	-	-	5	S
66	0	-	-	-	0	-	-	-	-	-	-	-	0.5	-	-	-	205	5	0.5	0.5	0.5	D
67	-	-	-	-	1	3.5	-	-	-	-	-	-	-	-	-	-	45	3	-	-	3.5	S
68	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	2	84	4	-	-	5	S
69	-	-	0.5	1	-	-	-	-	-	-	-	-	-	-	-	-	65	4	-	-	4	S
70	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	39	4	-	-	6	S
71	0	3	-	-	-	-	-	-	-	-	2.5	3	-	-	0	3	85	6	-	4	7	S
72	-	-	-	-	1	-	-	-	-	-	2	4	-	-	-	-	120	4.5	4	4	7	D
73	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	3	57	3	-	-	5	S
74	-	-	-	-	0.5	2.5	-	-	-	-	-	-	-	-	-	-	46	3	-	-	3.5	S
75	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	55	4	-	-	6	S
76	-	-	-	-	-	-	-	-	-	-	2	3	-	-	0	3	105	6	-	-	6	S
77	-	-	-	-	-	-	-	-	-	-	0.5	1.5	-	-	-	-	40	4	-	-	4	S
78	-	-	1	1.5	-	-	-	-	-	-	-	-	1.5	-	1	-	138	6	1	1	1.5	D
79	-	-	-	-	-	-	-	-	-	-	-	-	2	-	2	-	49	2	-	-	3	D
80	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	2.5	85	4	-	-	5	S
81	-	-	0.5	-	0	-	-	-	-	-	-	-	-	-	-	-	85	4	-	-	1	D
82	-	-	0.5	1.5	-	-	-	-	-	-	-	-	-	-	-	-	40	3	-	-	3	S
83	-	-	-	-	1	2.5	-	-	-	-	-	-	-	-	-	-	69	3	19	19	24	S
84	-	-	1	2	-	-	-	-	-	-	1	2	-	-	1	2.5	68	4.5	-	-	4.5	S

MASTER CHART

SL. NO	Low Voltage		ST elevation		Inverted T		Prolonged PR Interval		Atrial fibrillation		Extra systole		Ventricular tachycardia		QTc Prolongation		Treatment					
	A	N	A	N	A	N	A	N	A	N	A	N	A	N	A	N	At	Pr	V	ICU	HS	O
85	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	3	38	4	-	-	5	S
86	-	-	-	-	-	-	0.5	3.5	-	-	-	-	-	-	-	-	65	4	-	-	6	S
87	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	3	44	3	-	-	5	S
88	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	125	4	0.5	0.5	0.5	D
89	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	3	64	4.5	-	-	6	S
90	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	5	36	3	-	-	7	S
91	-	-	-	-	1	3	-	-	-	-	-	-	-	-	1	3	65	4	-	-	5.5	S
92	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	39	4	-	-	6	S
93	-	-	1	2	-	-	-	-	-	-	-	-	-	-	-	-	45	3	-	-	4	S
94	-	-	-	-	-	-	-	-	-	-	-	-	1	-	0	-	164	5	1	1	1	D
95	-	-	-	-	-	-	-	-	-	-	2	3	-	-	-	-	57	3	-	-	5	S
96	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	3	49	3	-	-	5	S
97	-	-	-	-	-	-	-	-	-	-	-	-	3	3	0.5	4.5	64	4	-	3	6	S
98	-	-	0.5	1.5	-	-	-	-	-	-	-	-	-	-	0.5	1.5	88	4	-	-	5	S
99	0	-	-	-	-	-	-	-	-	-	-	-	1	-	0	-	145	5	1	1	1	D
100	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	74	4	-	-	6	S
101	-	-	-	-	-	-	0.5	2.5	-	-	-	-	-	-	-	-	53	3	-	-	4	S
102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	4.5	37	4	-	-	6	S
103	-	-	-	-	-	-	-	-	0.5	1	-	-	-	-	-	-	70	4.5	-	-	4	S
104	-	-	0	1	-	-	-	-	-	-	-	-	-	-	1.5	3	40	4	-	-	5	S
105	-	-	-	-	2	4	-	-	-	-	-	-	-	-	-	-	43	3	-	-	4	S
106	0	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	110	5	0.5	0.5	0.5	D
107	-	-	0	1.5	-	-	-	-	-	-	-	-	-	-	3	5	38	3	-	-	5.5	S
108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	3	74	4	-	-	5	S
109	-	-	1	2.5	-	-	-	-	-	-	-	-	-	-	1	2.5	105	4	-	-	6	S
110	-	-	-	-	0.5	2.5	-	-	-	-	0.5	2.5	-	-	-	-	78	4	-	-	4	S
111	-	-	0.5	2	-	-	-	-	-	-	-	-	-	-	-	-	47	3	-	-	3.5	S
112	-	-	-	-	-	-	-	-	-	-	-	-	2	-	0.5	-	90	4	-	1	2	D

KEYS TO MASTER CHART

TYPE OF EXPOSURE

IE - Intentional Exposure

AE - Accidental Exposure

AGENTS USED

DM - Dimethoate

MP - Methyl parathion

BK - Bug killer liquid

CP - Chlorpyrifos

MC - Monochrotophos

FN - Fenthion

QP - Quinolphos

DC - Dichlorofos

MODE OF CONSUMPTION

PA - Poison + Alcohol

PW - Poison + Water

AL - Poison alone

PM - Poison + Milk

Ot - Other modes eg: mixing with food etc

CLINICAL FEATURES

P	- Pinpoint pupils		
M	- Depressed mental status		
S	- Secretions	+	Mild
		++	Moderate
		+++	Severe
F	- Fasciculations		
C	- Convulsions		
RF	- Respiratory Failure		
IMS	- Intermediate syndrome		
BP	- Blood pressure		

ECG CHANGES

A	- Appearance (days after admission)
N	- Normalization (days after admission)

TREATMENT

At	- Atropine total dosage needed		
Pr	- Pralidoxime dose needed per day		
V	- Ventilator support started (days after admission)		
ICU	- Intensive care unit started (days after admission)		
HS	- Hospital stay duration in days		
O	- Outcome	S	Survival
		D	Death

ABBREVIATIONS

ACh	- Acetyl choline
AChE/ChE	- Acetyl cholinesterase
ACTH	- Adrenocorticotropic hormone
AF	- Atrial Fibrillation
ARDS	- Adult respiratory distress syndrome
ATP	- Adenosine triphosphate
CNS	- Central Nervous System
CCU	- Coronary care unit
ECG	- Electrocardiograph
ICU	- Intensive care unit
M/F	- Male/Female
NTE	- Neuropathy Target Esterase
OP	- Organophosphorus
PAM/P2AM	- Pralidoxime (Pyridine-2-aldoxime methyl chloride)
RBC	- Red blood cell
VT	- Ventricular Tachycardia
WHO	- World Health Organisation